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ORIGINAL CONTRIBUTIONS

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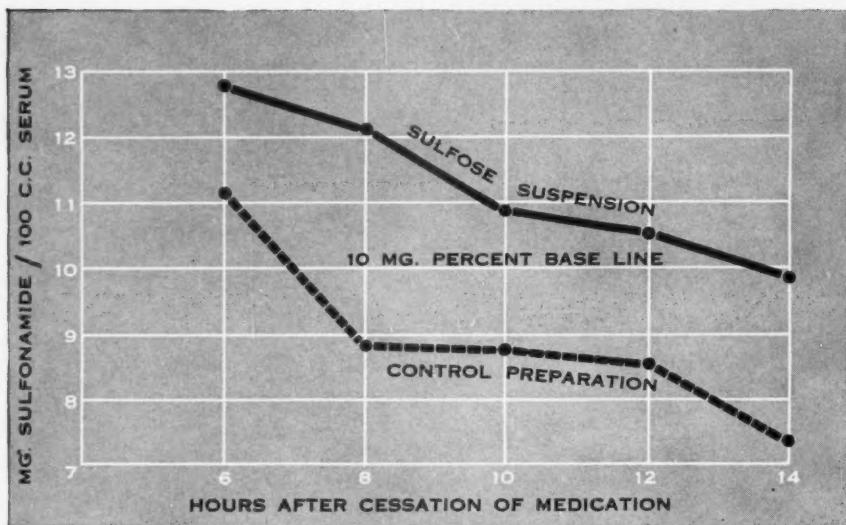
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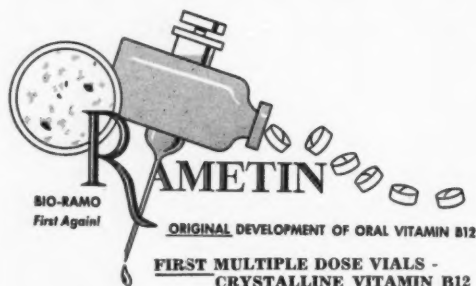
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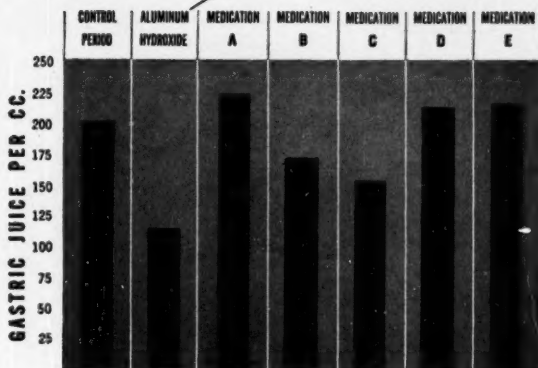
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*Steigmann, F., and Schlesinger, R. B.: A Resin-Gastric Mucin Mixture in the Medical Management of Peptic Ulcer, *American J. Dig. Dis.* 17:361-365 (Nov.) 1950.

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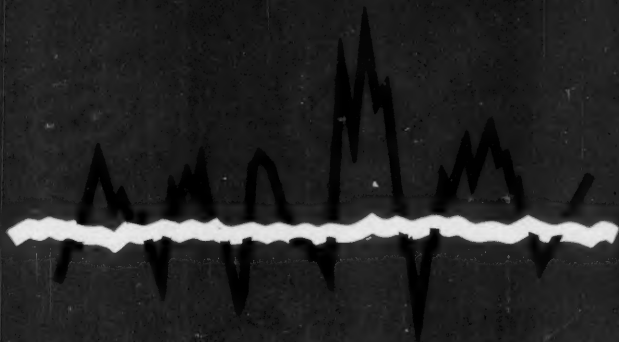
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THE PHENOMENON OF CHYLOMICRONS IN FAT ABSORPTION AND ARTERIOSCLEROSIS

H. NECHELES, M. D., Ph.D., F. A. C. P. Chicago, Illinois.

THE OPINIONS OF biochemists and physiologists on the mechanism of fat absorption have been and are still in a state of flux. Before 1900, the belief prevailed that fat was absorbed in both, the unsplit and the split state. From 1900 up to recently, Pflügers view that total hydrolysis is necessary for absorption of fat, has dominated. His theory has been supported by such authorities as Henriques, Bloor, Verzar, and others, until Frazer (1) reopened the question. He has shown that fat can be absorbed in two ways, as unsplit fat, and as fatty acids; the unsplit fat goes into the lymph, while the fatty acid is resynthesized into fat in the epithelium of the small intestine from where the portal blood carries it to the liver. Frazer's theory of two different pathways of fat absorption has been criticized (2). To me, the most important criticism appears to be that, contrary to Frazer's statement, ingestion of fatty acid can lead to systemic lipemia and chylomicronemia, and that absorption of fatty acids after oral administration is delayed, probably due to irritation of the small intestine by the fatty acid. However, Frazer has supported his theory of dual fat absorption by a body of additional experimental results, which have not been disproved. He has demonstrated that food fat, stained red with sudan, was found only in the chyle and in the fat depots, but not in the liver; that systemic lipemia following oral feeding of fat could be depressed by the addition of lipase; that, if the intestinal lipase was inhibited by a detergent, sodium cetyl sulfate, the absorption of fat was not prevented. Frazer's theory is supported by Mellanby's (1) earlier findings in the cat, in which, peculiarly, lipase is produced only in the pancreas and not in the intestine. Yet, if the pancreatic secretion of the cat was drained from the body, absorption of fat was still rapid. A further support of Frazer's theory lies in the old observation that, if large amounts of specific fats are fed, the same are found in the fat depots of the body.

The intestinal mucosa excretes fats and cholesterol into its lumen, the larger part of which is reabsorbed. The ingestion of fatty acids may intensify reabsorption of excreted fat, and this fact must be checked carefully, before the important results of Frazer's work can be disproved.

My laboratory has been working with chylomicrons for the last 3 years (3,4), and I am going to review our earlier and our recent results. In view of the

bearing that our previous findings may have on phenomena of fat metabolism, nutrition of the aged, and arteriosclerosis, we have spent the last 2 years with rechecking our former results and extending our work.

At this point we should define the terms used for fat globules in the blood. The term chylomicron is used for the globules plainly and clearly visible in the dark field with oil immersion and 950 X magnification. We have observed that, in fasting specimens and in the serum of a case of sprue after a fat meal, the chylomicrons were quite small as compared to those in the serum of a normal person following a fat meal. We have counted all of these bodies and not, as Frazer and others, only the large or shining ones. This we did, because we observed that a shining chylomicron could change into a dull one, and vice versa. The smallest chylomicrons have been called lipomicrons by some. We propose the name of lipomicrons for all bodies in the blood similar to chylomicrons, but which are so small that it is impossible to count them in the dark field. Chylomicron counts are difficult, and the method is subject to errors. In the case of counts above 400, dilution must be used, and grave errors can accrue from that. Frank and Ingelfinger (5) have stated, that a progressive increase of chylomicrons counts occurred with progressive dilutions of the serum. Such error would invalidate our published results in the older age groups. We have, therefore spent much time checking the factor of dilution. Serum with high concentrations of chylomicrons was used, which still could be counted and rechecked without dilution. These sera were then diluted and the chylomicrons were counted in the dilutions. Triple distilled sterile water and 20 and 40% urea solutions were used as diluents. Painstaking cleanliness of all glassware was found to be absolutely essential. With this technic we have found, that dilutions can be used for counting chylomicrons and that the counts were the same and were reproducible within acceptable limits of errors. We have thus not been able to confirm Frank and Ingelfinger. Unfortunately, these authors did not mention what type of diluent was used, nor did they describe the technic employed. Thus, we feel that the counts in which dilutions had to be used in our previous and in our present work were correct within the limitations of the method.

We have performed 4 series of chylomicron studies on a group of 12 young and on a group of 12 old people. The ages of the younger group varied between 20 and 30 years, with an average of 24 years. The ages of the older group varied between 68 and 83 years, with an average of 75 years. Two different levels of fat intake were used, namely 0.25 and 0.5 grams of fat per kilogram of body weight, because we felt that, as far as the chylomicron count is concerned, tolerance to larger amounts of fat might be different from tolerance to small amounts of fat. We have used also, in addition to chylomicron counts, a nephelometric mea-

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Department of Gastro-Intestinal Research, Medical Research Institute of Michael Reese Hospital.

Submitted Feb. 20, 1951.

Aided by the Abbott Fund and by the Jacob Meyer Old Age Research Fund. The laboratory is in part supported by the Michael Reese Research Foundation. The experimental work on chylomicrons was performed by Drs. G. Becker, R. Greenspan, and L. Marder; the chemical analyses were performed by Dr. B. Maizel. The complete report of our work will appear soon.

surement of the Tyndall effect of serum, as proposed by Moreton (6,7). The latter author has stated that both, the chylomicron count and the nephelometric method, measure the concentration of chylomicrons. This, we were not able to confirm. Our own results indicate, that the nephelometer measures light refraction from chylomicrons and from corpuscular bodies smaller than chylomicrons (lipomicrons). Some of these smaller bodies can be seen in the dark field as fine, ill defined shadows. We have good reason to believe that also smaller elements, Gofman's (8) macromolecules of 30-70 Svedberg units increase the nephelometer readings. In many tests, both, chylomicron counts and nephelometer curves ran parallel, in many other tests they diverged widely. This latter observation we believe is due to the presence of large numbers of lipomicrons, in addition to chylomicrons. Thus, the nephelometer readings depend on the dispersion of corpuscular fat in the serum, whether as chylomicrons or whether as smaller bodies. The nephelometric method may have advantages, because the values obtained may parallel the values for neutral fat in the serum closer than the chylomicron counts. It is possible on the other hand that only the large elements, the chylomicrons, play a role in the genesis of arteriosclerosis.

The average values of chylomicron counts to meals of 0.25 grams and 0.5 grams of fat per kg of bodyweight in a group of young and in a group of aged subjects were compared. In the old subjects the curves were much higher and the duration of chylomicronemia was longer than in the young subjects. A comparison of the nephelometric curves of the young and the aged groups indicated that the differences between these groups were not as significant as the differences between the chylomicron curves. This indicates to me, that the dispersion of fat in the blood of young and of old persons is different, with a relative prevalence of the larger elements, the chylomicrons, in the blood of the older subjects, while the concentrations of the smaller elements, the lipomicrons, may be larger in the young group. The curves indicate that, with the meal of 0.5g of fat per kg of body weight, the counts of the old group stayed up, at the 6 hour period, while those of the young group were going down. We cannot tell from our present data, how long the chylomicronemia in the older subjects lasted beyond 6 hours.

Psychic tension and physical exertion appear to affect the chylomicron counts, as described already by Gage and Fish (9), and as noted in our earlier publication (3,4). These elements were not controllable entirely in our tests, and their degree may have varied in our earlier and in the present series. We suspect also that variations in weather and air pressure affect chylomicron and nephelometric curves.

We have tried to control smoking during our tests, but we may have failed in this in a number of subjects. As noted earlier (3,4), smoking was found to elevate the chylomicron counts and the nephelometer readings very markedly in young subjects. Thus, there are a number of important factors that appear to affect the chylomicron counts in the blood, and some of these factors are hard to control.

Hueper (10) has demonstrated the damaging effects of macromolecular substances in the blood on the

arterial intima, and he has suggested that these effects may initiate and develop the arterial lesions of arteriosclerosis. He has proposed that macromolecular substances form a surface film on the intima and prevent sufficient oxygenation of that membrane. Moreton (6,7) has advanced the idea, that chylomicrons in the circulating blood are thrust on the intima with every pulse wave and that many penetrate this delicate membrane. He assumed that chylomicrons contain cholesterol and that, while the neutral fat component of the chylomicrons disappeared rapidly, cholesterol remained and accumulated, leading to deposits, formation of foam cells, calcification, and ulceration, in other words, to the arteriosclerotic lesion. I believe we have strengthened Moreton's theory by showing higher chylomicron curves in aged subjects. We have also found high chylomicron and nephelometer values in a small number of subjects with hypertension and in children with the nephrotic syndrome.

Moreton (6,7) has stated that chylomicrons contain cholesterol, but to our knowledge he has not published any proof of this fact. Frazer's work does not indicate the presence of cholesterol (1) in the chylomicrons. Dr. Gofman has informed me that chylomicrons contain approximately 5% of cholesterol.

We have devoted much effort to answer this question. We were favored by the cooperation of the Samuel Deutsch Serum Center of Michael Reese Hospital, which supplied us with concentrated chylomicrons obtained in the preparation of human plasma. The substance has the physical appearance of oleomargarine and the taste of butter. Upon dispersion in water, it yields tremendous chylomicron concentrations, indistinguishable from normal chylomicrons. Chemical analysis of washed chylomicron fat shows that it contains 10-12% of sterols. Using the standard method for determination of cholesterol, i.e., precipitation with digitonin and treatment with acetic anhydride, approximately 80% of this sterol was found to be cholesterol, 65% of the cholesterol was in the ester form.

An ether extract of the chylomicron fat, which contains both the sterols and the neutral fats, did not contain any phosphorus. Neither did a chloroform extract of the water phase which remained after the ether extraction show the presence of phosphorus. From these findings we can assume that no free lecithin, cephalin, or sphingomyelin, is associated with the chylomicrons.

The saponification number of the chylomicron fat was 185. Cramer and Brown (19) have reported a saponification number of 195-198 for human depot fat.

No water soluble fatty acids could be detected in the chylomicron neutral fat, and it contained no or very little monoglycerides.

The aqueous residue from the ether extraction of the chylomicron fat was of a mucilaginous nature, and it always contained phosphorus. For each gram of chylomicron fat extracted, the aqueous layer contained 1.3 to 1.7 mg of phosphorus.

The unusual stability of the chylomicron is associated with the material which coats the surface of the fat globule. This material appears to be a protein (as assumed by Frazer) which goes into the aqueous phase during extraction of the chylomicron fat. Thus, while upon dispersion, chylomicron cream

yields chylomicrons even after repeated centrifugation at high speeds, the ether extracted lipid material of chylomicrons does not.

Thus, we are back at the thesis, that chylomicrons may cause arteriosclerosis. If they do, prevention or at least depression of high chylomicron counts appears to be logical in a trial to prevent the disease. A lipase preparation depressed chylomicronemia in aged subjects considerably, practically to the levels of the young group (3). The lipase did not affect the chylomicron curves of young subjects significantly but, curiously, Tween 80 raised the chylomicron curves of young subjects to high levels (3).

We have a few patients, that had suffered a coronary infarct, on lipase management for one year. The patients are living and well, but the small number and the short period of observation do not warrant reporting details now.

I feel that there is a need for theories on the genesis of arteriosclerosis, which are based on honest observations. The physicians will be able to choose among these, and they will formulate a method of therapy according to the theory they favor. Thus, medical progress may occur.

Gofman (8) has made a splendid contribution to this field. However, like in the case of chylomicrons or nephelometer units, not every one of his normal cases had low values of macromolecules of 10-20 S. U., and not every one of his hypertensive subjects had high values. His results, as ours, have only statistical value. We know that the same dose of a drug per kg of body-weight will produce the same effect only in a percentage of experiments, never in all of them, because we are dealing with varying sensitivities not only in different subjects, but even in the same subject. Thus, I have to leave it open, which is the agent responsible for

arteriosclerosis, molecules of cholesterol of S.U. 10-20 of Gofman, or chylomicrons, or a number of other agents reported in the extensive literature.

Maybe it is none of them, but we at least feel that we are contributing to the expansion of knowledge by analysis of phenomena, which must have a meaning.

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CHRONIC ULCERATIVE COLITIS—CLINICAL AND BACTERIOLOGIC RESPONSE TO AUREOMYCIN*

MICHAEL H. STREICHER, M. D.* AND MR. ROBERT KNIERING** Chicago, Ill.

AS IN ALL SCIENTIFIC pursuits in clinical medicine one invariably becomes tenaciously attached to the study of some entity yet unconquered. At this writing, after many years physicians are still searching for specific treatment for one of the most dreadful diseases in the abdomen, chronic ulcerative colitis. Until the early years of the twentieth century all reports on the subject were very discouraging. It has been the opinion of most gastro-enterologists that the treatment of colitis was limited to that of the specific forms of ulcerative colitis and that the diagnosis of the non-specific form was based on the existence of colon ulcers with negative bacteriologic observations with extensive anatomic changes of the colon.

*Associate Professor of Medicine, University of Illinois.

**Research Assistant in Medicine.

***The aureomycin was supplied for these studies through the courtesy of Lederle Laboratories.

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Thorlakson (1), Hurst (2) and Einhorn (3) refer to this entity as being primarily due to bacillus of dysentery. Yeomans (4), Bassler (5) and Lynch (6) consider the disease to be of infectious origin. Logan (7), Buie (8) and Bagen (9) however stated that ulcerative colitis was of bacterial origin and maintained that the diplostreptococcus was the specific etiologic factor.

In 1926, Streicher and Kaplan (10) began extensive clinical and experimental studies on ulcerative colitis and reported that all bacteria present in the colon during the course of this disease were responsible causative factors. Their results show that in most cases of ulcerative colitis the diplostreptococcus is frequently found in association with other bacterial flora such as hemolytic streptococci, diphtheroid bacilli, staphylococcus albus and aureus, staphylococcus albus hemolyticus, bacillus pyocyaneus, B. lacti-aerogenes and B. coli.

It is quite obvious that in addition to the presence of severe infection, there is associated a marked loss

TABLE I. BACTERIAL COUNTS OF STOOLS BEFORE AND AFTER ORAL ADMINISTRATION OF AUREOMYCIN

Name of Organisms and Counts in Millions (Per gram of stool)										
No. of Patients	Coliform		Staph. Albus		Strept. A.		Strept. B.		Strept. G.	
	Before	After 7b 14b	Before	After 7 14	Before	After 7 14	Before	After 7 14	Before	After 7 14
25	55a	17 5 23	10 5	19	9 5	20	8 5	38	17	9

a—Bacterial count in millions.

b—Number of days on aureomycin

in weight, diarrhea, cramping in the abdomen and a loss of body fluids so that the nutritional reserves of the individuals are rapidly depleted. One also encounters the problem of remissions or recurrent exacerbations of ulcerative colitis.

We are therefore faced with a patient who has a severe infection of the colon, one in a very poor nutritional state, and who by reason of the type of infection is exposed to acute exacerbations of the disease process. Extensive clinical observations with vaccine therapy did not obviate the acute exacerbations and recurrences and that active or passive immunization was not conferred.

The introduction of therapy with the sulfanilamide and its derivatives was hailed as a step in the right direction and while miraculous results were recorded at the onset, it was finally established that the specific action exhibited by certain sulfonamides was limited in scope and that the action was bacteriostatic against the secondary bacterial invaders (11).

The recognition of penicillin as a general antibacterial agent was referred by the experiments of Fleming (12) in 1929. More extensive clinical studies proved penicillin to exert property against gram positive bacteria aerobe or anaerobe, and only some anti-bacterial property against many gram negative organisms. Fleming (12) also reported penicillin to be relatively ineffective against organisms of the colon typhoid group.

A constant and continued search for an antibiotic that would be effective against a wide variety of bacteria, both aerobic and anaerobic, gram positive and gram negative resulted in the discovery of aureomycin by Duggar (13). Schoenbach (14) stated that pharmacologic studies revealed that aureomycin was active when the antibiotic was administered orally and that it possessed a low degree of toxicity. Spink and Yow (15) refer to the fact that aureomycin therapy is particularly indicated in the treatment of infections resistant to penicillin, streptomycin and the sulfonamides.

PROCEDURE OF STUDY

Fifty patients afflicted with chronic ulcerative colitis were employed in this study; of these 18 were males and 32 females. All were studied clinically and procto-

scopically. Aureomycin (Thrice recrystallized) was administered orally to each patient in doses varying from 3 to 6 capsules (250 mg. each) daily. The majority of the patients were hospitalized for two weeks and controlled during the experimental trial. Studies of levels in the blood, urine and stool were determined daily. Bacteriologic studies were made before and after treatment.

RESULTS

Bacterial Response—The bacteriologic response in the stool to oral administration of aureomycin is significant in that the *B. coli* count, the staphylococcus aureus, streptococcus alpha, streptococcus beta and streptococcus gamma counts are all decreased progressively and correspondingly.

For instance, with a daily dosage of 6 capsules of aureomycin orally, the *B. coli* was recorded as 50,000,000 before treatment and 25,000,000 four days and 19 hours after treatment; the staphylococcus albus count was decreased from 17,000,000 to 10,000,000; the streptococcus A was decreased from 20,600,000 to 12,200,000; the streptococcus B was decreased from 15,800,000 to 9,800,000 and streptococcus G from 32,000,000 to 19,000,000.

The results exemplified in detail in table 1 show the bacteriologic response to aureomycin in 25 patients covering a period of 1 to 14 days.

Determination of aureomycin levels in the blood, urine and stool. The levels of aureomycin in the blood, urine and stool were determined by the method of Lederle Laboratories. The blood samples were drawn daily and were collected sterilely. Serum is used for the level determination.

Individual specimens of urine are obtained each morning at 9:30 A. M., the urine is diluted 1:10 with nutrient broth and used for level determination. One gram of stool is used for the bacteriology assay. Six to eight cc. of sterile distilled water is added and 1 cc. of the above sample is used for level determinations. The level of aureomycin in the blood varied from .05 mcg. per cc. to 1.6 mcg. per cc. over a period of 14 days on oral daily administration of 6 capsules. The level of aureomycin in the urine varied from .0125 mcg.

TABLE II. SHOWING THE NUMBER OF PATIENTS AFFECTED BY UNTOWARD SYMPTOMS

No. of Patients	Nausea	Vomiting	Burning on Urination	Headaches	Itching Skin Rash	No effect
50	12	10	3	6	6	13

per cc. to 1.5 mcg. per cc. over a period of 14 days. The level of aureomycin in the stool varied from .0125 mcg. per grain to .4 mcg. per gram.

CLINICAL STUDIES

This study was carried on for one year. Of the 50 patients treated orally with aureomycin 32 were female and 18 were male; of these 23 were in the chronic stage and 27 in the acute stage. The majority of the group showed improvement with oral administration of aureomycin in doses of 3 to 6 capsules (250 mg. each) daily. The impression obtained is that the patients are benefited to the extent that the cramping in the abdomen subsides, that the discomfort in the abdomen is alleviated and that the number of evacuations are reduced. A small percentage of the patients have been disturbed by nausea and occasional vomiting after oral intake of aureomycin; some complain of burning on urination or headache; however, this varies with the particular preparation used (see Table 2 listing the untoward effects in 50 patients). The stools become more formed, not odorless and the blood in the stool is reduced considerably; the color also changes to a lighter yellow.

The entire group was studied proctoscopically after treatment but the changes are not pronounced enough to evaluate accurately. In general one may say that on direct visualization there is evidence of some improvement in the resistance of the colon mucosa to ulceration upon direct trauma.

DISCUSSION

If we assume from the bacteriological observations of Bergen (16) that chronic ulcerative colitis is an infectious disease, then the rationale of the specific treatment lies in the active immunization against the causative organism. The causative organism in our opinion is not a single type of bacteria, but a number of different types of bacteria, or a number of strains of the same bacterium, so that we are not justified in assuming that a green-producing gram positive diplostreptococcus is solely responsible for the disease. Again, patients of ulcerative colitis who receive hypodermic injections of an autogenous vaccine made from a pure culture of green producing diplostreptococcus show little or no progress, whereas the same patients injected with a polyvalent vaccine present encouraging results. The autogenous vaccine in use at that time was usually made from cultures obtained from the colon of patients through the proctoscope.

Many investigators believed that the univalent or polyvalent vaccines have the properties of non-specific protein therapy. That this is not true is demonstrated by the fact that negative results were obtained when typhoid vaccine or milk injections were substituted in these cases.

The fact that vaccine therapy did not obviate the acute exacerbations and the repeated recurrences of symptoms proved conclusively that the vaccine therapy was not specific and that active immunization was not conferred in this method of treatment.

The introduction of therapy with the sulfanilamides and its derivatives was received with relief, but while miraculous results have been recorded at the onset, the use of these drugs in the treatment of this disease was nevertheless considered hazardous. Their specificity of action on infectious disease due to streptococcus hemolyticus has been established, but only a small percentage of patients with ulcerative colitis harbor this type of streptococcus strain, so that its applications were limited. Our experience concerning the use and evaluation of sulfanilamide and two of its derivatives (11) are recorded in table 3. On sulfanilamide all the acutely ill patients became worse; vomiting ensued, diarrhea became exaggerated, blood appeared in the stool in larger amounts than usual and cramping in the abdomen became severe. Azosulfamide merited more favorable results, it was possible to use it parenterally during periods of suspension of oral administration. Such after effects as eruptions on the skin, nausea, vomiting, jaundice, and diarrhea were observed on many occasions. At that time we considered sulfathiazole to be the least toxic of the sulfanilamides.

Specific activities exhibited by certain sulfonamides and its derivatives against various bacteria have become well known to the profession. This action of this group of drugs was regarded as primary; the sulfonamides produced a reduction in the bacterial rate of growth. It is evident from the voluminous literature on these antibiotics that the improvement recorded in their use in infectious diseases of the colon is due to the fact that these agents are bacteriostatic against the secondary invaders and that in this manner the defense mechanism of the patient is increased against the primary infection.

In recent years sulfaguanidine, sulfasuxidine, and sulfathalidine have been the three agents most widely used in the management of infectious disease of the

TABLE III. SHOWING EVALUATION OF SULFANILAMIDE AND ITS DERIVATIVES

	Type of Colitis		Results		
	Acute	Chronic	Good	Fair	Poor
Sulfanilamide	12	5	2C x	1C	12A xx 2C
Azosulfamide	22	14	4A 2C	1A 1C	17A 11C
Sodium Sulfathiazole	9	6	3A	4C	6A 2C
Patients in each Group	43	25	7A 4C	1A 6C	35A 15C
Total Number of Patients	68		11	7	50

x C—Chronic Ulcerative Colitis
xx A—Acute Ulcerative Colitis

colon. Sulfathaladine (phthalylsulfathiazole) is similar to succinyl sulfathiazole chemically and therapeutically but is more effective. Poth and Ross (17) have reported that sulfathaladine is absorbed sparingly from the gastrointestinal tract, that it maintains low concentrations in the blood (.1 to 1.5 mg) and that it is rapidly excreted in the urine (5%). It is our impression that sulfathaladine proved to be less toxic and more bacteriostatic than any intestinal agent used previously, and that daily doses of 3 gms. taken orally brought about the desired therapeutic effect in infectious diseases of the colon.

The recognition of penicillin as a general antibacterial agent was demonstrated by the experiments of Fleming (12) in 1929. More extensive clinical studies proved penicillin to exert property against the many gram negative organisms. Fleming also reported penicillin to be relatively ineffective against organisms of the colon typhoid group.

A constant and continued search for an antibiotic that would be effective against a wide variety of bacteria, both aerobic and anaerobic, gram positive and gram negative resulted in the discovery of aureomycin by Duggar (13).

Schoenbach (14) stated that pharmacologic studies revealed that aureomycin was active when the antibiotic was administered orally and that it possessed a low degree of toxicity. Spink and Yow (15) refer to the fact that aureomycin therapy is particularly indicated in the treatment of infections resistant to penicillin, streptomycin, and the sulfonamides.

While aureomycin has been found therapeutically to be active against a broad spectrum of bacteria, it is recognized that organisms vary in their susceptibility to this antibiotic. Oral aureomycin is absorbed very readily and therefore is well adapted for ambulatory patients.

It has been found that aureomycin is most effective when used in the presence of actively reproducing bacteria and that bacterial resistance to this antibiotic is not developed easily. These properties of aureomycin are evaluated to a great extent in the treatment of chronic ulcerative colitis.

There is conclusive evidence of bacterial response to aureomycin demonstrated in this group of patients with ulcerative colitis; there is a gradual and progressive decrease in the numerical count of the bacteria studied; this coupled with a general clinical improvement of these patients over a period of 14 days would indicate that aureomycin administered orally is beneficial in chronic ulcerative colitis. Being that ulcerative colitis is a disease process of prolonged duration, interpolated by remissions and exacerbations, administration of any form of medication would of necessity extend over prolonged periods; any antibiotic therefore which is employed in the management of ulcerative colitis should possess properties free of toxic effects which would render the agent suitable in this requirement.

In our studies we were also interested in determining whether or not aureomycin is primarily bacteriostatic or bactericidal; in directing our studies beyond 14 days, this question too, would be more easily qualified.

CONCLUSIONS

1. Aureomycin administered orally is effective in chronic ulcerative colitis.
2. The bacterial response to aureomycin is favorable but its limitations are not completely established.
3. Aureomycin may be used in ulcerative colitis to advantage.

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DIABETIC COMA* PROBLEMS OF FLUID AND ELECTROLYTE BALANCE

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THE PROBLEMS OF FLUID and Electrolyte Balance in Diabetic Coma are the problems of dehydration, ketosis and acidosis. They are also the problems of pathogenesis, therapy and prevention of diabetic coma, because it has become quite evident that the disturbances in water and electrolyte metabolism play a far more significant role in this diabetic emergency, than hyperglycemia and glycosuria.

This paper will be concerned with a discussion of the following three aspects, which appear to be of main interest to the practicing physician:

- 1) the origin and extent of fluid and electrolyte imbalance in diabetic coma and the correlation of the biochemical changes with the clinical signs and symptoms,
- 2) the role of hyperglycemia in the development of water and electrolyte loss and acidosis, and the vicious circle by which diabetic coma is precipitated and
- 3) coma treatment and the possible dangerous side-effects of insulin: hypotatemia and hypoglycemia.

I.

Origin and extent of fluid and electrolyte imbalance in diabetic coma are best appraised by following a patient lapsing into this state.

Assuming our patient is a known diabetic, then his hyperglycemia and glycosuria will have been under control either by diet alone, or by insulin, or by diet and insulin. His food and water intake probably are adequate, evidenced by weight constancy and equilibrium between fluid intake and output.

Gradually, however, our patient experiences increased thirst and increased diuresis. We can infer that his blood sugar is rising and his glycosuria increasing. He develops headaches and feels drowsy; in spite of increased fluid intake, he becomes unable to keep pace with his fluid output. This water deficit becomes greater, when nausea interferes with quenching of his thirst and when vomiting causes additional loss of fluids. Headache, drowsiness and nausea are not symptoms of hyperglycemia, but of dehydration. Yet from here on, the disturbance is no longer confined to dehydration alone; the increased glycosuria has also caused increased urinary excretion of salts, especially of sodium and chlorides. The loss has been aggravated further by

the vomiting. Nausea and vomiting persisting for several hours will also interfere with food intake and thus with energy metabolism. Our patient goes now in the state of starvation. With no food being ingested, the organism turns to its own sources for energy and begins to burn fat and, to a lesser degree, protein. Fat oxidation leads to ketone body production, and protein catabolism to the release of nitrogenous substances, phosphates and other breakdown products. These appear in the bloodstream and are either utilized by the peripheral cells or excreted through the kidneys. Since the rate of production may be greater than the rate of utilization or excretion, these substances begin to accumulate in the bloodstream. This is especially true for the ketone bodies which as acids require neutralization. At this point, our patient is in ketosis, has become more drowsy and fatigued, and begins to complain of abdominal pains and cramps. His skin and mucous membranes now are dry, his eyeballs are soft and sunken, his abdomen may be distended and tender, his pulse is small and weak, his blood pressure low, his reflexes are sluggish, and his temperature probably subnormal. Soon, the initially normal or shallow respiration changes to the classical rapid and deep type of Kussmaul breathing, and a sweetish odor, due to acetone, becomes noticeable in his breath. By now, the patient is in frank acidosis; the drowsiness further increases and the patient lapses into deep coma and shock.

This process developed over a period of hours or even days; diabetic coma usually develops slowly through the stages of dehydration, starvation, ketosis and acidosis. This clinical course is accompanied by characteristic biochemical changes, which in the fully developed state of diabetic acidosis can be summarized as follows: in the blood the CO_2 combining power is markedly decreased, usually below 15 Vol. %, the pH lowered from the normal of 7.4 to around 7.1; the serum sodium has fallen from a normal of 140 mEq/L, to about 120 mEq/L, while elevated serum levels are obtained for potassium (above 4 mEq/L), magnesium, phosphates, sulphates and non-protein nitrogen; the blood sugar level as well as the blood ketone level are high; dehydration and hemoconcentration are evidenced by an elevated hematocrit value and by an increase in the number of circulating red and white blood cells, although the high white cell count may be only in part due to hemoconcentration. The urine is acid, scanty, of high specific gravity, smells of ammonia and contains large amounts of sugar, ketone bodies, chlorides, sodium, potassium, phosphates, sulphates, and protein.

Were we able to examine the intracellular fluid as well as the intravascular fluid and the urine, we would find a decrease in potassium and magnesium concentration, perhaps an increase in sodium, a high sugar and ketone acid level, a lowered pH, a decrease of fluid, and an increase in cellular breakdown products as nitrogenous metabolites, sulphates and phosphates.

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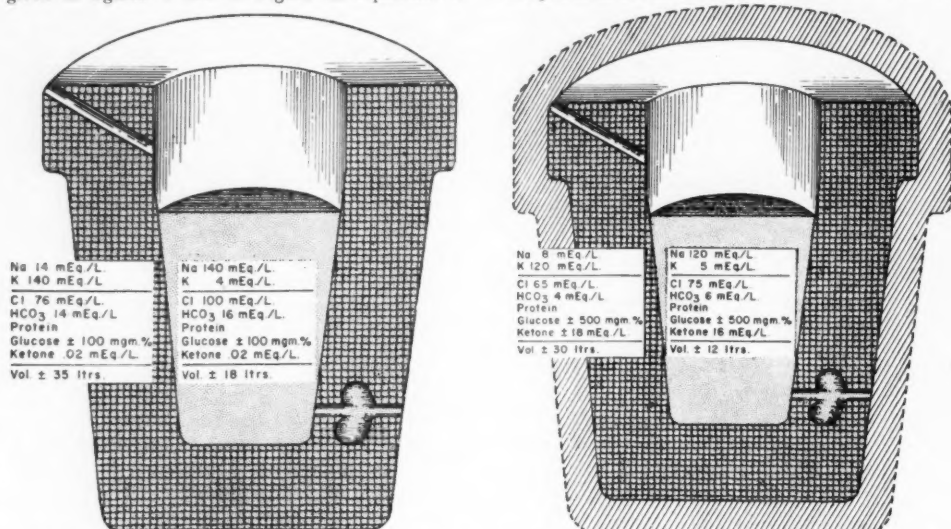
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The overall loss of fluid and electrolytes of a patient in diabetic acidosis for more than 24 hours can be estimated as about 7000 cc of water, or 10% of his body weight, 8 to 9 gms. of sodium and chloride respectively, and more than 10 gms. of potassium.

A schematic representation of these changes is given in figures 1 and 2. Figure 1a represents a

diagrammatic sketch of fluid and electrolyte contents in the extracellular and intracellular compartments of a normal individual. Superimposed upon this physiological state, figure 1b demonstrates graphically the overall decrease in body mass due to dehydration. The extracellular compartment as well as the intracellular compartment are affected and to some extent, the cell



Figures 1a and b.: Schematic representation of intracellular and extracellular fluid compartments in health (a) and in diabetic coma (b).

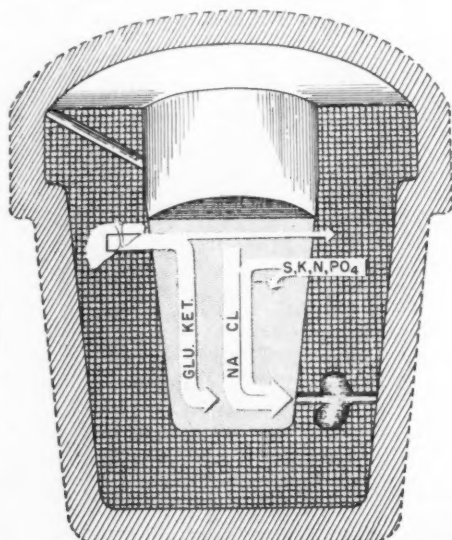


Fig. 2.: The shift of electrolytes and glucose in the various fluid compartments in diabetic coma.

mass itself, which has decreased due to cell destruction and catabolic processes. Fig. 2 shows the accumulation of glucose and ketone bodies; the disproportion between their rate of production and rate of utilization or excretion; the shift of the electrolytes Na, K, and Cl in both fluid compartments; and the rise of nitrogenous metabolites and phosphates in the body fluids.

We turn now to the correlation of signs and symptoms with biochemical changes. It has been recognized generally that a fairly good agreement exists between the severity of the clinical condition and those laboratory data which reflect changes in fluid and electrolyte metabolism. Equally apparent however has been a lack of correlation between signs and symptoms and the degree of hyperglycemia and glycosuria, except for the fact that glycosuria is generally present and that the blood sugar is elevated. It can be said that the severity of a diabetic coma can be estimated fairly well from the degree of dehydration and acidosis but not at all from the height of the blood sugar or the amount of glycosuria. Indeed, the same blood sugar level may be found in the same diabetic patient once when he is critically ill with acidosis and coma and at another occasion when he seemingly enjoys good health, bothered by nothing more than thirst and polyuria.

If it is remembered, however, that the diabetic patient passes into coma and acidosis through the

stages of dehydration, starvation and ketosis then it should not be surprising that these complications and their signs but not the underlying disease determine and dominate the clinical course. Indeed, there seems to be no more but a quantitative difference between the starvation ketosis of the non-diabetic and the acidosis of the diabetic. Yet, we still hear that the precipitating cause of diabetic coma is not starvation but rather dietary indiscretion, overindulgence in starchy food; and the attending hyperglycemia is given as proof for this indictment!

II.

What, then, is the role of hyperglycemia in the development of dehydration and acidosis?

To appraise this problem it may be worth-while to recall three clinical observations:

1) Glucose infusions to non-diabetic patients, as given so often for intravenous alimentation, never affect significantly the acid-base balance or cause acidosis, though hyperglycemia, glycosuria and increased diuresis develop.

2) If a previously well-controlled diabetic is permitted to increase his carbohydrate intake without increasing his insulin dose, he certainly will develop hyperglycemia and glycosuria, yet seldom will there occur a significant acid-base disturbance or acidosis.

3) The same patient, however, will lapse rather quickly into coma with the accompanying disturbances of fluid and electrolyte metabolism if his insulin dose is decreased or withheld without any change in his diet.

What does this indicate? In the normal individual, fed glucose intravenously, the hyperglycemia is evidently produced by offering more glucose to the organism than can be stored or metabolized under optimal physiological conditions. Glycogenesis in the liver and glucose oxidation in the periphery proceed at optimal rate — the excess glucose, however, remains in the blood and is excreted in the urine. Some water and salt may be lost — but not enough to interfere with cellular metabolism.

A similar situation apparently applies to the diabetic patient whose diet has been increased without an increase of his basic insulin dose. His carbohydrate metabolism still operates satisfactorily, although its impairment is indicated by the fact that hyperglycemia occurs at a carbohydrate intake which a normal individual would tolerate without elevation of the blood sugar. As soon as insulin is withheld, however, the control breaks down and the biochemical changes, which lead ultimately to coma, become unavoidable.

Thus it appears, that we deal with two types of hyperglycemia—one due to availability of carbohydrates over and above the amount which must be utilized in order to prevent excessive fat oxidation and ketone formation; the other due to inadequate utilization of carbohydrate so that there is need for excess fat. Their distinguishing factor is the amount of available insulin.

We must conclude then, that not "hyperglycemia per se" precipitates water and electrolyte imbalance severe enough to cause coma, but only that hyperglycemia, which is the result of insulin deficiency. This insulin deficiency, in turn, must be severe enough to retard glycogenesis and glucose oxidation below a minimal level. It must be a "critical" insulin deficiency.

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Critical insulin deficiency leads to decrease or arrest of glycogenesis and increase in fat oxidation, to hyperglycemia and ketone body-accumulation in the blood, to increased diuresis, glycosuria and ketonuria. It further leads to a decrease of the alkali reserve, and acidosis; also to cellular catabolism which aggravates further the loss of electrolytes and their shift from the intracellular to the extracellular fluid compartment.

Critical insulin deficiency may develop spontaneously. This is the case, when the insulin production in the pancreatic islet cells falls below the critical level. It will, of course, develop too, when the diabetic patient omits to take the required dose of insulin. The critical situation, in these two instances, is the result of an absolute decrease in available insulin. It may, however, result as well from a relative insulin deficit; this happens when the insulin sensitivity decreases while its production or dose have remained at the same level. Such loss of efficiency may be due to the action of endocrine antagonists or more rapid inactivation. A previously adequate secretion or dose of insulin may then become critically insufficient. It is well known that relative insulin deficiency develops in the presence of many complicating diseases as for instance infections, hyperthyroidism, gastrointestinal diseases, trauma or surgery. As soon as these complications come under control the pre-existent insulin sensitivity is restored and the insulin requirement returns to its previous level.

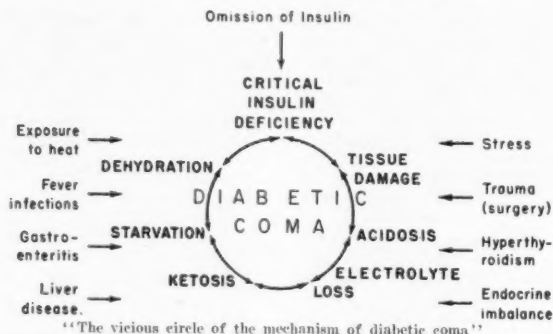
It is interesting to note that these complicating diseases, different as they are, have more in common than only to cause insulin resistance. All are situations of stress. All of them for various reasons, cause dehydration, starvation and electrolyte loss in the non-diabetic as well as in the diabetic. There is good reason to assume that these changes in water and electrolyte metabolism are responsible for a decrease in insulin sensitivity again in the non-diabetic as well as in the diabetic. The non-diabetic can make the necessary adjustment by increasing his insulin secretion; the diabetic on the other hand is unable to do so; he cannot step up his insulin production, his previously adequate insulin supply becomes critically deficient and this in turn enhances dehydration and starvation metabolism and leads to more severe ketosis and frank acidosis and coma.

Thus we find a perfect setting for a vicious circle in the development of diabetic acidosis. On one hand the failure to meet a minimal insulin requirement may start the process through loss of water and electrolytes to acidosis and coma, but on the other hand dehydration and starvation as manifestations of complicating diseases may be the starting points and may cause critical insulin deficiency with further deterioration of water and electrolyte metabolism. Such a vicious circle is represented in fig. 3, which shows the complicating diseases with their predominant metabolic effect and the various steps through which the circle runs, from wherever it may have been entered. Only adequate therapy can interrupt this course and prevent the imminent disaster.

III.

Coma treatment and the possible dangerous side-effects of insulin: hypopotassemia and hypoglycemia.

The aim of every therapy is 1) to remove the cause of the disease and 2) to make such replacements and



adjustments as are necessary to re-establish physiological function. Removal of the cause is an absolute necessity; the need for replacements and adjustments is relative and depends as much on the responsiveness and reaction of the affected organism as on the causative agent.

In coma, critical insulin deficiency is the common denominator of whatever the precipitating causes may be. Adequate insulin administration is therefore the foremost therapeutic essentiality, especially since the other contributing causes usually are not removable as easily and as rapidly as desirable. Nevertheless, treatment must be directed against them too as soon and as vigorously as possible.

Not less essential is the replacement of those substances, which were lost during the phase of development of coma, and which are required immediately or very soon in order to assure physiological function; here we think mainly of the replacement of fluid and salts to overcome dehydration and shock and of the administration of glucose as a source of energy as soon as it can be utilized for this purpose.

Less essential are those adjustments or replacements which in most instances can be left to the responsiveness of the affected organism itself and which are done in due time. In this category belongs the early administration of bicarbonate, of intracellular electrolytes as potassium and magnesium, or the replacement of nitrogen to rebuild the lost protein.

Since decreased insulin sensitivity is an outstanding feature of diabetic coma, insulin must be given not only promptly, but in large, and if necessary, in ever-increasing doses, until its effect is affirmed by improvement in the general condition of the patient, by decrease of blood sugar, ketonuria and glycosuria. It cannot be emphasized strongly enough that there does not exist any absolute insulin insensitivity, but doses as high as 3000 or 5000 units may be required to overcome the initial insulin resistance. As a general rule, an initial dose of 100 units of a quick-acting insulin should be doubled at hourly intervals until a response is noted.

To appraise the essentiality of insulin, it must be remembered, that it exerts its effect not only on the blood sugar but also — though indirectly — upon water and electrolyte metabolism. By again permitting the utilization of glucose it stops ketogenesis. The blood level of ketone acids will fall. They no longer enter the blood stream in excessive amounts, yet their urinary excretion as well as the peripheral utilization continues.

Consequently, base will no longer be required for the neutralization of the ketone acids and will be free for restoration of bicarbonates. The alkali reserve in the blood increases and by the same token, the CO_2 combining power as well as pH of the plasma rise and approach normal levels. The decreasing acidosis diminishes cellular catabolism. Cells cease to disintegrate thus arresting the release of nitrogenous breakdown products and of electrolytes as potassium and magnesium, into the extracellular fluid spaces. Phosphorous will now be used again for the phosphorylation of glucose and its excretion will therefore diminish. With sugar re-entering the cells and there being transformed into glycogen or burnt to CO_2 and water, the hyperglycemia will, of course, decrease; fluid will return into the cells, and thus alleviate in part the cellular dehydration. In the liver, glycogenesis is accompanied by the re-entering of potassium into the cells consequently the potassium blood level will fall too and its urinary excretion will diminish.

Hypoglycemia and hypopotassemia are the two dangers of rapid and vigorous insulin treatment; against them the body must be protected. Insulin acts over a period of several hours, thus its effect will accumulate, if it is given at hourly intervals. This accumulated effect is intended and desired to overcome the initial insulin resistance, but it will persist far beyond this time, unless protective measures are taken.

Of the two dangers of insulin treatment, the hypoglycemic reaction is imminent in almost every instance and may develop suddenly and rather early, while the hypopotassemia develops slowly and rather late.

Hypopotassemia is seen almost exclusively in those instances where insulin treatment is accompanied by rapid and massive administration of fluids. Then the potassium blood level is lowered not only by the action of insulin, but also by dilution. Symptoms of potassium deficiency usually occur when the serum concentration is lower than 2 milli-equivalents per liter. They are manifested by muscular weakness and by myocardial damage, as evidenced in the electrocardiogram by low voltage, lowering and lengthening of the T wave, depression of the ST segment and prolongation of the QT complex. In an attempt of substitution therapy with potassium it is important to remember that hypopotassemia, serious as it may be, is less dangerous than hyperpotassemia, which may cause immediate cardiac arrest. Therefore, the rapid intravenous replacement of potassium is fraught with greater danger than

the deficiency state itself, especially if renal function is impaired and excess potassium cannot be excreted rapidly. Although a number of multi-electrolyte solutions containing potassium have been developed recently for intravenous use, their application, is recommended only in the presence of good renal function and the infusion should be made very slow. In most instances, intravenous administration can be avoided at all and potassium can safely be given by mouth in the convenient form of orange juice, which is rich in this electrolyte. Since potassium deficiency develops rather late, the patient will usually have been aroused from coma and will well be able to retain oral alimentation.

Hypoglycemia on the other hand, is more hazardous than hyperglycemia. If permitted to persist for some period of time, it will cause irreversible damage to brain and myocardium. The only means to prevent this danger is the administration of glucose. Much has been said about the abuse and harmful use of glucose in coma treatment; the impact of this criticism, however, is directed not against glucose itself, but against its ill advised administration at too early a time and in too massive dose, so that the organism cannot benefit from it. There is no evidence that glucose is harmful if given judiciously. Obviously, in order to counteract over-activity of insulin, it ought not be given before evidence of insulin activity has been obtained either by urinalysis or by blood sugar determination; the falling blood sugar and the decreasing glycosuria, however, are proof for

the fact that glucose can be used again for the energy metabolism, and that it is time to guard against hypoglycemic reactions. The judicious use of glucose therefore must be based upon due consideration of the organism's need for energy as well as of its capability to utilize glucose. The energy requirement of a resting adult man can be estimated as 60 to 80 calories per hour or an equal of 15 to 20 grams of glucose. The capability for utilization depends, of course, on the amount of administered insulin. Since this had to be given liberally and in cumulating doses, an additional 5-10 grms. of glucose per hour should be in place over and above the minimal requirement. Thus, we arrive at a total of about 25 grms. per hour. We have used with good results intravenous infusions of 5% glucose in saline at a rate of 120 drops per minute. This infusion is started routinely as soon as we find a decrease in glycosuria. At that time, we place this solution instead of a saline venoclysis which was instituted immediately when coma treatment started. The glucose infusion is then continued until the patient is able to be fed by mouth. Such management will prevent unexpected hypoglycemia, will provide insulin with a substrate to act upon and thus help to cut down fat oxidation and ketogenesis. It also will not interfere with the re-establishment of physiological fluid and electrolyte balance. Such interference, however, will occur, if glucose is given too early, too rapidly or in too large quantities. Then, indeed, the only result will be a new rise in blood sugar and glycosuria with all

TABLE I.

THE ESSENTIALS OF THE TREATMENT OF DIABETIC ACIDOSIS

WHAT	WHY	WHEN	HOW	BEWARE
ESSENTIAL				
INSULIN	to start glycogenesis to stop ketogenesis to stop diuresis	immediately	100 U Reg. or Crystal- line insulin double previous dose every hour until response	Hypoglycemia Hypopotassemia
Isotonic saline solution	to replace fluids to replace Na, Cl	immediately	intravenously, 2-3000 cc 120 drops 1 min.	renal function overhydration
Plasma	to combat shock to replace fluid and electrolytes	if pt. does not respond to saline	intravenously 600 cc	Hepatitis (late)
Glucose	to supply energy to prevent insulin- hypoglycemia	as soon as glycosuria de- creases	intravenously 5% in saline	increase of glycosuria increase of water and electrolyte loss
NOT ESSENTIAL				
Bicarbonate	to combat acidosis (to accelerate the function of insulin)	when above measures are ineffectual	intravenously, 500 cc 4% sod. bicarb., Ringer's solution, Hartmann's	alkalosis if renal function impaired
Potassium	to replace K loss	late, not before blood sugar has started to drop	best, by mouth (orange juice)	Hyperpotassemia in renal impairment
Multi-electrolyte solutions	to provide optimal fluid and electrolyte replacement in the presence of renal impairment	to follow saline when renal impairment	Darrow's, Butler's solution intravenously	overdosage of electrolytes

accompanying changes of further dehydration and increased loss or shift of electrolytes.

Essential next to insulin administration is the replacement of fluids and salts.

Intravenous administration of isotonic sodium chloride solution, started simultaneously with the initial injection of insulin, is the first step and frequently the only one necessary, to overcome dehydration. It is well recognized that an isotonic sodium chloride solution is by no means a physiological solution; not only is its sodium chloride ratio unphysiological, it is also lacking totally in all other essential electrolytes, especially potassium and magnesium which are so important for the intracellular fluid compartment. It must be remembered, however, that the immediate therapeutic concern is the hemoconcentration and the shock, both involving primarily the extracellular compartment.

Isotonic saline supplies the extracellular space with the most needed water, sodium and chlorides. The excess chlorides will be excreted readily, if the renal function is not seriously impaired. In spite of the fact that large quantities of saline have to be given, the dangers of toxic effects due to overhydration or alkalosis are rather remote. Since the coma patient may have lost up to 10% of his body weight in fluids an equal amount may have to be replaced within the first 24 hours.

If saline solution fails to arouse the patient from circulatory failure, one may have to resort to blood or plasma transfusion. Then the possible risk of a late transfusion hepatitis must be accepted in view of the greater danger of prolonged shock.

A review of the essential and non-essential steps in the treatment of fluid and electrolyte imbalance in diabetic coma is given in table I.

Only a few words should be added about alkali

therapy, which is listed among the non-essential procedures. It has been pointed out above that the organism in diabetic acidosis has not incurred any actual loss of alkali: the bicarbonate space has been taken over by the neutralization of ketone acids. It will be freed again as soon as, under the influence of insulin, the ketobodies disappear from the blood. Alkali administration does not seem to accelerate this effect of insulin. Nevertheless, observations are on record, which suggest that in exceptional cases coma treatment became successful only after alkalis had been added to all other therapeutic procedures.

It is beyond the scope of this discussion to emphasize in detail the special emergency care which every coma patient requires. It must suffice to summarize that the patient should be under constant supervision, that he be kept warm and that a gastric lavage be carried out as soon as possible. No other medical emergency calls for as integrated team work of physician and nurse as diabetic coma.

SUMMARY

1. Diabetic acidosis and coma develop through the steps of dehydration and starvation; its severity is proportional to the degree of fluid and electrolyte imbalance.
2. Diabetic acidosis and coma are not precipitated by hyperglycemia itself, but only by that type of hyperglycemia which is due to critical insulin deficiency.
3. Critical insulin deficiency may be caused by various mechanisms; these constitute a vicious cycle leading to coma and acidosis.
4. The need for large doses of insulin, for fluid replacement and judicious use of glucose in coma treatment is emphasized.

SAINT'S TRIAD: HIATUS HERNIA, DIVERTICULOSIS COLI AND GALL STONES

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IN 1948 MULLER (1), reporting from Johannesburg, drew attention to a triad of hiatus hernia, diverticulosis coli, and gall stones. This combination of commonplace entities was found in three patients, and Muller named it "Saint's triad" in favor of his colleague, Professor Saint of Cape Town, who had first mentioned the possible clinical importance of the association.

After the appearance of Muller's paper, two cases were encountered in quick order, and others have since been noted. In order to study a growing feeling that Saint's triad must be rather common, the records of patients with hiatus hernia examined during 1950 in the Gastrointestinal Clinic at Walter Reed Army Hospital were reviewed. In 31 such patients the investigation had included gall bladder and colon roentgeno-

grams in addition to upper gastrointestinal x-rays, or the record contained information of surgical findings which satisfied the only criterion, that all three organs in question had been adequately investigated. It was found that there had been five cases representing Saint's triad among the 31 patients. Among the other 26 patients with hiatus hernia, the additional studies had shown only one case of diverticulosis coli and one of cholelithiasis.

CASE I.

A 55 year old white woman had not been well since the birth of her first child 20 years previously. She had had post-partum eclampsia at that time. Two years later a hysterectomy was done because of uncontrollable bleeding. Within six months she had developed intestinal obstruction, and at operation it was found that diverticulitis of the transverse colon had been responsible for obstructive adhesions about the mid-jejunum. The gall bladder with several stones was removed later that same year, following an episode of obstructive jaundice. Now, 19 years later, the patient complain-

From the Gastrointestinal Section, Walter Reed Army Hospital.

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ed of an excess of gas and a feeling that food was catching and remaining high in the epigastrium. There had been a few spells of nocturnal vomiting. The weight had been steady and there had been no recognized bleeding from the gastrointestinal tract. Physical examination showed a pleasant, rather healthy appearing middle age woman. Except for the surgical scars, there were no remarkable findings. In the course of study it was found that the patient had rather extensive diverticulosis coli and a moderately large sliding hiatus hernia. Esophagoscopy revealed no esophageal complications. The patient was treated symptomatically.

CASE II.

A 62 year old white man was hospitalized because of abdominal pain which had occurred about a half-hour after meals for 15 years. The patient sought help at this time because of increasing severity in the symptoms, although the simple pattern had shown no change. The presence of two large gall stones had been known for nine years, but the patient had refused surgery. Four years previously he had had a small gastrointestinal hemorrhage and studies at that time showed a hiatus hernia. The gall bladder was eventually removed. Physical examination showed an obese florid male with pulmonary emphysema and mild hepatomegaly. Roentgenographic studies demonstrated a fixed 4 cm hiatus hernia, and gastroscopic examination revealed a small ulcer on the posterior wall of the flated sac. In view of the findings to date, a barium enema was done even though the patient had no symptoms referable to this part. Diverticulosis was found in the descending and sigmoid colon.

CASE III.

A 53 year old white woman was studied because of patternless epigastric pain and vomiting of 5 years' duration. It eventually became evident that the symptoms were on the basis of a marked conversion hysteria, but during the course of study x-ray examination revealed the presence of a small para-esophageal hiatus hernia, a poorly functioning gall bladder containing stones, and diverticulosis of the transverse and descending colon. In addition, the roentgenologist pointed out a calcification within the left ovary. It was felt that all of the demonstrated organic disease was of sub-clinical importance.

CASE IV.

A 54 year old white soldier was examined to determine eligibility for disability retirement. He had an 8 year history of epigastric pain and pyrosis, but had never sought medical help. There were no other symptoms of significance, and examination suggested no important disease. A barium enema showed several diverticula in the distal portion of the descending and sigmoid colon. Upper gastrointestinal x-ray studies revealed a moderate sized hiatus hernia. In view of these findings, the gall bladder was investigated and stones were found radiologically. Esophagoscopy and gastroscopic evaluation of the esophagus and herniated portion of the stomach showed no mucosal disease.

CASE V.

Fifteen years previously this 56 year old white man had had a cholecystectomy following three episodes of acute gall bladder colic; he was told that his gall bladder contained "a hand-full of stones." He had then been well for three years, when left lower quadrant aching pain led to x-ray studies and the diagnosis of uncomplicated diverticulosis coli. Ten years prior to the present admission a diaphragmatic hernia had been repaired surgically, and one year later bilateral inguinal hernias were repaired. Five years prior to admission he complained of epigastric pain, and x-ray studies suggested an ulcerated lesion just below the gastric cardia. At laparotomy, however, no ulcer was found but instead a small recurrent hiatus hernia with regional post-operative distortion. The patient was hospitalized now because of weakness and black stools. A rather severe hypochromic anemia was found, and stools were positive for blood. A barium enema showed diverticulosis, and upon upper gastrointestinal fluoroscopy at least half of the stomach was seen above a widely patent diaphragmatic hiatus. Gastroscopic study limited to the herniated portion of the stomach showed no secondary mucosal disease. It was felt, nevertheless, that the bleeding was secondary to herniation of the stomach and the diaphragm was repaired for the third time.

COMMENT

One would be hard put to justify an assumption that there may be some basic causal significance in the association of these common diseases. Other combinations of apparently unrelated abdominal diseases are frequently encountered and tendencies in this direction have been spoken of from time to time. A frequent association of diverticulosis with hiatus hernia would be explainable if congenital weakness be accepted as causally important in both, but cholelithiasis is another matter. There is nothing to be gained by speculating on a common etiology because the individual etiologies are poorly understood. But, however it may be explained, if the triad is common, it would behoove the physician to be rather skeptical of accepting one demonstrated entity as the explanation for the patient's symptoms. Saint's triad was common, indeed, in the small series reviewed here. Surprising was the observation that the triad was found in five patients, but two of the entities were present in only two patients.

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PHARMACOLOGICAL PROPERTIES OF A NEW ANTISPASMODIC N,N-DIMETHYLTHYMYLOXYACETAMIDINE HYDROCHLORIDE

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THIS PAPER PRESENTS the results of an extensive study of the pharmacological reactions of the most active of a group of amidines exhibiting antispasmodic potentialities. The potency of N,N-dimethylthymyloxyacetamide hydrochloride (Su-198) in the various pharmacological preparations employed and also its toxicity have been compared with cor-

responding figures for the following known antispasmodics: Trasentine, Trasentine-6H and atropine sulfate. Some of the corresponding figures have been included for the less active diethyl congener of Su-198, Su-216. The discerned relations between chemical structure and this pharmacologic property have been previously discussed (1).

METHODS

All methods employed in this study have been previously described in detail (1) except for the preparation

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TABLE I.
COMPARATIVE ACTIVITY OF ANTISPASMODICS ON VARIOUS ISOLATED TISSUES
(All doses in micrograms)

Drug	Action On Perfused Feline Heart		Toxicity I. V. LD ₅₀ (Rats) (5)	Ileum of Guinea Pig (Doses microgm./cc.)		Ileum of Rabbit vs. BaCl ₂ (3) (microgm./cc.)
	Dose	% Inhibition (4)		vs. Histamine (1)	vs. Acetylcholine (2)	
Su-198	100	12	46	10	0.3	70
Su-216	50	9	38.4	10	4	50
	100	16				
Trasentine	100	14	27	20	8	70
	200	17				
Trasentine- 6H	50	5	37	10	2	25
	100	16				
	200	25				
Atropine	100	8	100-125	150	0.05	1000
	300	14				

- (1) The minimal dose inhibiting at least 95% of the spasm normally induced by 0.6 microgm./ml. of histamine dihydrochloride; in this and the following two tests the drug was added two minutes before the stimulating drug.
 (2) The minimal dose inhibiting at least 95% of the spasm normally induced by 0.2 microgm./ml. of acetylcholine hydrobromide.
 (3) The minimal dose, added at the height of the response, relaxing the spasm induced by 300 microgm./ml. of barium chloride.
 (4) Expressed as average % decrease in amplitude in at least two experiments.
 (5) 2% solution; 30 seconds for injection. (Doses expressed in mgm./kgm.)

of a cat for the study of the action of the drugs on the salivary secretion, the nictitating membrane, and the pupil. For this preparation the method previously described by Yonkman and his associates was employed (2, 3).

RESULTS

Table No. 1 presents the results obtained in the study of this drug's action on various isolated tissues.

Dogs with Thiry-Vella loops were employed for studying in vivo the intestinal effects of the drug. Those with loops exhibiting high levels of spontaneous motility were used to permit the measurement of a general antispasmodic action rather than the more specific action that would have been measured had a spasmogenic agent such as histamine been administered prior to the antispasmodic. The present compound was studied repeatedly in five different dogs in doses of

0.1 to 0.5 mgm./kgm. Figure 1 is typical of the records so obtained. The inhibition of the segmental movements varied from nine to about twenty-six minutes and was not seemingly correlated with the size of the dose. The inhibition of the tonal changes usually outlasted that of the segmental movements and varied from eighteen minutes to half an hour or more. The lower doses did not alter the animal's respiration or cardiac rate, but the highest dose employed not infrequently gave a brief but significant tachycardia. It was hoped that some quantitative measure of the drug's effectiveness might be obtained from these studies, such as the average dose inhibiting the intestinal movements for a specified period. These figures, however, prove much too variable, a result not surprising in the light of the many variables affecting the responses of the intact gut (4).

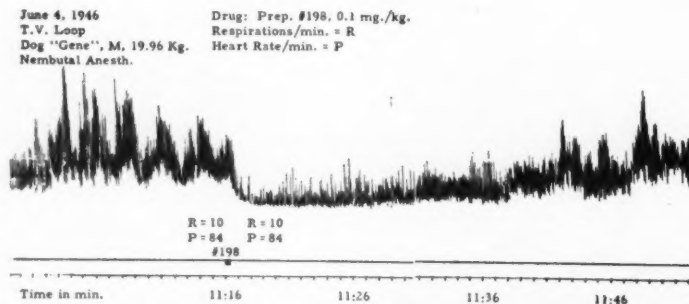


Figure 1. 0.1 mgm./kgm. Su-198 given at 11:16 effected a sharp drop in the tonal level of the gut. Both the segmental and the peristaltic movements were inhibited. The former, as usual, returned sooner than the latter.

TABLE II.
COMPARATIVE ACTIONS OF SPASMOLYTICS ON INDICATED FUNCTIONS

(All doses microgm./kgm. unless otherwise noted, and injected intracarotidly unless I. V. is noted. They represent minimal doses eliminating the function, unless qualified by "I", which signifies only partial inhibition)

Drug and (No. of cats studied)	FELINE SALIVATION (Doses in Microgm.)		VAGAL & VASCULAR (Doses in mgm./kgm.)		NICITATING MEMBRANE CONTRACTIONS		
	Pilocarpine Induced*	Histamine Induced**	CTF (Chorda Tympani Faradization)	Vagal Block (Faradization Peripheral Cut Nerve)	Mecholyl Block*** (Doses I. V.)	Pilocarpine Induced* (Doses in microgm.)	Spontaneous Activity (Doses per kg.)
193 (13)	100-200 (25-I)	200-300	100-300 brief	0.1-0.5	0.5-3.0	50-100	Less than 1 mgm. re- laxed; more than 1 mgm. stimulated
216 (4)	500-800	500-800	1500-2000 (2 hrs.)	0.5	2-4		0.1 mgm.—slight relaxation; 2 mgm. slight stimulation.
Trasentine (6)	500	500	500 (1.5 hrs.)	5	15	500	5 mgm.—brief relaxation
Trasentine- 6H (8)	5-10 Prolonged	10	5-10 Prolonged	1.5-2.0	1.5-2	10	1 mgm.—slight re- laxation; 1.5 mgm.— complete, brief relaxation
Atropine (9)	1-2	1-2	1-2 (More than 1.5 hrs.)	0.025	0.025	1-2	25 microgm.—slight relaxation

* 300 microgm./kgm. pilocarpine nitrate subcutaneously.

** The stimulating dose varied from 1.5 microgm./kgm. intracarotidly.

*** Refers to block of hypotensive action of 0.5 microgm./kgm.

tachycardia which usually persisted at a rate of 180-200 per minute for about an hour. Doses of 2 to 5 mgm./kgm. administered orally to dogs also gave tachycardia as the only symptom. These results suggested that tachycardia might prove the most common side effect in humans. The actual side effects experienced by ten human volunteers who took the drug were dryness of the mouth and moderate interference with vision. These side effects occurred in doses of from 20-40 mgm. (total dose) dependent upon the weight of the volunteers. Only volunteers weighing less than 130 pounds experienced side effects after 20 mgm.

CHRONIC

Young mature male and female rats of an inbred Wistar strain were divided into five groups, with five males and five females in each of the first three groups, and ten males and ten females in the last two groups. The first three groups received respectively 5, 10 and 20 mgm./kgm. injected intraperitoneally five days a week for three months. The fourth group initially received a 0.5 per cent concentration of the drug in ground feed, and the fifth group twice that concentration in the feed. These concentrations were later reduced to 0.1 per cent and 0.25 per cent, because of the marked weight loss resulting from a diminished food intake which was presumably occasioned by the bitterness of the drug.

The following hematological studies were made on all rats: erythrocytic, leukocytic, and differential counts, and determinations of hemoglobin and hematocrit. These studies were repeated on all rats at the end of the experiment, and, in addition, were performed on one male and one female from each group half way

through the experiment. At the end of the experiment the rats were sacrificed to secure tissues for histological study. At autopsy the tissues appeared grossly normal, save for some abdominal adhesions secondary to the intraperitoneal injections. The histological studies revealed no pathological changes (1). The hematological studies yielded values within normal limits.

Eight dogs comprised of four males and four females were divided into four groups with one male and one female in each group. The first group served as controls. The remaining three groups received respectively 2.5, 5.5 and 7 mgm./kgm. given twice daily per os five days a week for three and a half months. The following hematological studies were performed at the beginning and end of the experiment, and in addition on the 53rd and 99th days: erythrocytic, leukocytic and differential counts and determinations of hemoglobin and hematocrit. A renal function test was performed on one dog in each of three groups at the beginning and end of the experiment (phenolsulfonphthalein). An hepatic biopsy of one dog of each group was made at the beginning and end of the experiment. At the end of the experiment the two dogs receiving the highest dose and one dog receiving the intermediate dose were sacrificed and tissues were taken for histological examination. The histological and hematological studies gave results within normal limits. All the dogs remained in good health throughout the experiment, save for one that developed sarcoptic mange that yielded successfully to treatment, and a second dog that developed hemorrhagic enteritis which responded satisfactorily to sulfaguanidine. As adjudged by the tests used, renal and hepatic function were unaltered by the experiment.

Although all tissues had appeared normal at autopsy

the subsequent histological examinations suggested that two of the livers exhibited a little more fibrous tissue than normal. The nuclei of the renal tubular cells from these two dogs also seemed hyperchromatic. Although these minor changes could have been a reflection of the animals' ages or dubious dietary history before reaching our laboratories, it seemed advisable to clarify the cause. Accordingly, one male and one female in the original group of dogs were again fed the drug for thirty days. Both were given 10 mgm./kgm. per os twice a day. Previously the female had been given 5.5 mgm./kgm. twice a day and the male 2.5.

A PSP test of renal function was performed on the animals before and at the end of the thirty-day period. Results were within limits for both dogs. An hepatic biopsy of each dog was taken at the beginning of the thirty-day period and compared with liver sections subsequently secured at autopsy at the end of the experiment. The usual hematological studies were performed. All hematological values were within normal limits at the end of the thirty days. The liver sections from the two dogs were entirely normal at both the beginning and the end of the experiment. It was, therefore, concluded that the earlier minimal changes noted did not reflect a toxic action of the drug.

DISCUSSION

The evaluation of antispasmodics at present would appear to be largely impressionistic, although a recent publication (5) is a step toward the goal of a purely objective evaluation.

It would appear that an ideal antispasmodic would be more or less equally potent in antagonizing at least three different types of smooth muscle spasm: that induced by histamine, by acetylcholine, and by barium chloride. The mechanism of action of this last spasmogenic agent is unknown and its value is still widely disputed, but it is none the less true that antispasmodics presently available are quite effective in antagonizing its action. Drugs of unusually high anticholinergic specificity such as atropine will probably suffer from the same limitations in use as does that drug.

The respective doses inhibiting salivation and paralyzing the vagus were carefully determined, since they would appear to be measures of the extent to which dryness of the mouth and tachycardia might be anticipated as side effects in the human.

With the experimental data secured, various empirical equations were formulated, incorporating three basic sets of values: 1) measures of the spasmolytic actions of the drug (the antihistaminic activity, the anticholinergic activity, and the antibarium chloride activity); 2) measures of the side effects produced by the

drug (the dose inhibiting salivation and producing paralysis of the vagus in the cat); 3) measures of the drug's toxicity (the LD₅₀ in rats and the dose inhibiting the activity of the perfused cat heart). Although none of the resultant equations seems to have convincing validity, it may be possible to devise one after more extensive clinical trials of the drug. Even now the three measures referred to are obviously carefully evaluated by any investigator in an effort to decide whether a potential spasmolytic warrants clinical trial, but necessarily this process is largely subjective, and it is to be hoped that ultimately an empirical equation will be developed that will permit a more objective evaluation.

SUMMARY

1. The activities of a new antispasmodic, N, N-dimethylthymoxyacetamide hydrochloride and of its diethyl congener have been compared with the corresponding activities of Trasentine, Trasentine-6H, and atropine sulfate in respect to the following: a. Antagonism of a histamine-induced spasm of the ileum of the guinea pig. b. Antagonism of an acetylcholine-induced spasm of the ileum of the guinea pig. c. Antagonism of a barium chloride-induced spasm of the small intestine of the rabbit. d. Actions on the feline uterus in vitro and in vivo. e. Actions on the nictitating membrane of the cat and on salivation induced by drugs and by stimulation of the chorda tympani nerve. f. Paralysis of the peripheral cut vagus in the cat. g. Antagonism of Mecholyl-induced hypotension in the cat. h. Intravenous LD₅₀ in white rats. i. Chronic toxicological studies in dogs and rats.

2. The effects of Su-198 upon the intestines of dogs with Thiry-Vella loops and upon the bronchioles of the perfused guinea pig's lung have been described.

3. Some of the problems have been discussed which must be solved before an objective evaluation of an antispasmodic becomes possible.

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THE CASE FOR ROUTINE PROCTOSIGMOIDOSCOPY (REPORT ON FIVE HUNDRED AND FIFTY EXAMINATIONS)*

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THE IMPORTANCE of routine proctosigmoidoscopy in all cases requiring a gastrointestinal survey can not be over-emphasized. Further, one would not be amiss to include this procedure, when feasible, in physical examinations both in private and hospital practice. Omission of adequate study of the distal portion of the gastrointestinal tract may be attributed to reticence on the part of the patient and in some instances to the physician who hastens to institute therapy on a precursory examination influenced by the patient's diagnosis of "piles." Of the latter, Rankin (1) states that that physician is unquestionably guilty of a sin of omission. McCutcheon and Baxley (2) quote Buie as having found 48.5% of 1073 rectal malignancies had been operated upon for conditions unrelated to the malignant lesion. A minimal requirement of all physical examinations is inclusion of proctoscopic and rectal digital study. No gastrointestinal survey is complete without proctosigmoidoscopy (3).

Predicated on the above, proctosigmoidoscopy is routine in the Gastrointestinal Clinic, O. P. D., of the Queens General Hospital. In this institution patients having principally ano-recto-sigmoid disorders are referred directly to the Proctologic Clinic without firstly having been observed by the Gastrointestinal Division. Hence, the report herein included is of observations on 550 unselected gastrointestinal patients referred from the General Medical Clinic because of symptoms of the digestive system other than those directly pertaining to its most distal segments. In this group 225 had ano-recto-sigmoid disease. Of the 225 patients eleven had carcinoma, four not being even remotely suspected of having same. These findings bear out the validity of routine proctosigmoidoscopy in, at least, all gastrointestinal surveys.

PREPARATION OF PATIENT

While under certain conditions it is conceded that no preparation is desirable, we find that for routine study it is advantageous to have the lower bowel thoroughly cleansed with decinormal saline enemas carefully and slowly taken until the return is clear. Subsequently that morning the patient reports to the clinic where he is instructed to remain on the toilet for about ten minutes prior to the examination.

PRECAUTIONS

Proctosigmoidoscopy should not be attempted without a thorough acquaintance with the anatomy of the pelvic contents, rectum and sigmoid. A knowledge of the status of the pelvic contents is particularly important in the female patient. These patients frequently have varying degrees of pelvic disease with resultant

adhesions between the pelvic organs and the proctosigmoid juncture, which then becomes fixed in position.

Uncooperative patients, fixed proctosigmoid junctures and obstruction due to strictures, tumors and nonreleasing spasms are our indications for interruption of the examination. An attempt to complete sigmoidoscopy in the presence of these contraindications could readily result in perforation. A sudden blanching of the mucus membrane is a warning sign that too much pressure is being exerted on the instrument and perforation might result. This tragic accident may occur in the absence of the aforementioned contraindications, even when the sigmoidoscopist is thoroughly experienced.

The paucity of reports of perforation during proctosigmoidoscopy may be explained (4) on two bases: a) "specialists see these cases infrequently and therefore do not consider the report of one or two cases important"; b) "pride or prevention of possible suit for damage."

Crohn and Rosenak (5) cite reports by Rumbaugh, Schmidt, Goldman, Menegaux, Brumbaugh and also Retzlaff of perforations that they had experienced or encountered in their practices. In this report Crohn adds perforations of the sigmoid that occurred on two occasions while he was the sigmoidoscopist. In both instances his patients were cooperative, the examinations were performed with ease, without strain or undue force and as routine procedures. The colon was not diseased in either instance. Crohn had used air insufflation and in the light of these tragic accidents we do not use that procedure in our clinic.

Some years ago, without using air insufflation, under conditions similar to those cited by Crohn, the senior author experienced a tragic accident in his private practice. No perforation was recognizable and the patient left the office apparently in good condition in the late afternoon shortly after sigmoidoscopy. He was routinely instructed not to use any laxatives nor enemas for at least 48 hours. That evening due to some rumbling in the abdomen, he decided that a high colonic irrigation would be of value and took it upon himself to have same administered by one of his friends who was a graduate nurse. About midnight he developed abdominal cramps but did not seek medical advice until late the following morning. At that time he presented the clinical picture of a ruptured viscus and peritonitis. Laparotomy revealed a rent in the sigmoid.

One of Crohn's cases left the clinic without complaining and he did not hear of the results of an exploratory laparotomy until several weeks later. Perforation during sigmoidoscopy may occur without the onset of symptoms of a ruptured viscus for several hours after the examination (4-5) and the accident may go unrecognized. However as a rule the instrument is described as "going up higher than usual," pain in the right shoulder often occurs and a scout x-ray film of the abdomen reveals a pocket of gas

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beneath the right diaphragm. Later the symptoms of peritonitis develop (4).

Rayner (6) and Jones (7) each reported on an injury to the rectum subsequent to faulty administration of an enema. One can only postulate as to the cause of the perforation in the case experienced by the senior author.

Andresen (4) reported on the study of 94 cases of perforation of the rectosigmoid during proctosigmoidoscopy. Two of this series occurred while he was carrying out the examinations. He states that he "once heard a well-known internist *callously* remark that such a perforation is an accident which may be expected to occur when internes and residents are learning how to use the proctoscope." Calloused remarks of that type may be expected from the uninitiated or those that conducted an occasional but fortunately successful, examination and thereby indicate their lack of appreciation of the sigmoidoscopists' problems.

TABLE I

INCIDENCE OF ANO-RECTO-SIGMOID DISEASE

Number with lesions	225	40.9%
Number free of lesions	325	59.1%
Total cases studied	550	100.0%

TECHNIQUE

The choice of examining table and the type of instrument may be left to the discretion of the operator. Under average conditions any ordinary examining table may be used (8). To avoid interference with the light system from any residual bowel contents, an instrument having the light on the outer end is advantageous. Using a hard rubber instead of metal instruments is advisable. In the event that a metal instrument is used, the operator must be cautious not to attempt to turn off the current while the instrument is still inserted lest the patient and examiner receive an electric shock. The patient may suddenly violently move and sustain severe injury from the inserted sigmoidoscope.

The patient can usually be best examined while in the knee-chest position, leaning towards the left shoulder, head resting with the left side of the face on the table and the spine completely relaxed and slightly concave. The patient is then properly draped and the examination started.

An external inspection followed by a digital examination of the anus and rectum are performed. The digital examination aids further study by introducing the lubricant into the anus and somewhat dilating the anal sphincters as well as revealing some necessary information. This is followed by anoproctoscopy preferably using the Brinkerhoff type of speculum. The sigmoidoscope does not serve well as an instrument for inspection of the anus and lower portion of the rectum. The sigmoidoscope is then well lubricated and inserted into the rectum with the obturator in situ. A sensation of roominess for the inserted portion indicates that the rectum has been reached. The obturator is then removed and direct inspection started. *Slight* pressure forward on the instrument besides the weight of the scope along with the operator's directional aid propels its passage into the sigmoid. Direct inspection is carried out during this time. Air insufflation is never used in this clinic.

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Spasms are usually overcome by swabbing the mucosa with a 25% magnesium sulfate solution and allowing same a few moments to release the spasms. By requesting the patient to rise slowly to a knee-elbow or slightly higher position, retained portions of enema solution will flow out through the sigmoidoscope and permit better inspection. This effect may also be obtained by using cotton-swabs for absorption. Slow and gentle pressure with a cotton swab will relieve mucosal puckering into the instrument.

OBSERVATIONS ON EXAMINATION

The various steps in the examination must be carefully conducted. Not infrequently one may observe pathological states on external examination that may be explained by internal lesions and vice versa. Further, a detailed history leading to a clinical impression of diabetes

TABLE II
OBSERVATIONS IN THE SERIES STUDIED

Observed Ano-recto- sigmoid Pathology	Asymptomatic		Symptomatic		Total
	30 int. 29 ext. 11 both	—70	16 int. 21 ext. 16 both	—53	
Hemorrhoids					123
Fibroma of rectum	1		1		2
Sigmoiditis	1		2		3
Proctitis	2		2		4
Proctosigmoiditis	2		6		8
Reduplication of mucosal folds	4		9		13
Atrophic mucosa	6		3		9
Congested mucosa without other observed pathology	5		4		9
Pruritus ani	0		1		1
Hypertrophy of mucosal folds	2		1		3
Skin tags without other pathology	7		0		7
Rectal prolapse	2		2		4
Fistula-in-ano	3		1		4
Hypertrophied papillae	5		2		7
Benign Clinically	8		5		13
Polypi benign but biopsy malignant	3		1		4
Clinically malignant	0		2		2
Fissures	1		2		3
Anal ulcer	1		1		2
Anal stricture	0		2		2
Spasms without other pathology	9		3		12
Kinked proctosigmoid	2		1		3
Chronic ulcerative colitis	2		3		5
Cryptitis	0		1		1
Clinical proctosigmoid malignancy	1		4		5
Polonidal cyst	1		0		1

Note—Several of the patients had more than one of the above disease entities.

mellitus or allergy may explain an existing pruritus ani sans any lesion of the anus other than perhaps some tissue excoriation caused by the finger-nails while scratching.

Most of the lesions to be mentioned or discussed have at various times been observed in the cases included in our series. Since the patients attending the clinic are with but rare exceptions adults, anomalous states have not been encountered. Anomalous varieties of the congenital internal or external ectopic openings, congenital narrowing of the anal canal and imperforated anus or rectum are usually corrected during early life.

(a) EXTERNAL AND DIGITAL

External examination reveals the presence or absence of external hemorrhoids, fistulae, condylomas, fissures, pilonidal cysts, anal excoriations, tumors, skin tags, hypertrophied papillae, ulcers and protruding rectum, polyps and internal hemorrhoids. Sphincter tone and

TABLE III

AGE INCIDENCE OF ANO-RECTO-SIGMOID DISEASE

Decade	2nd	3rd	4th	5th	6th	7th	8th	Total	Percent
Females	8	22	34	28	20	8	4	124	55.1
Males	4	16	22	20	22	8	9	101	44.9

tenderness, stenosis, rectal prolapse, impacted feces, contiguous extrinsic tumors and masses of foreign body or neoplastic origin can be determined on digital examination. This procedure serves the double function of determining the presence of lesions and dilatation with lubrication of the anal sphincter which somewhat eases the inspection by the instrumentation to follow.

(b) INTERNAL

Not unlike interpretation with other endoscopy, the interpretation of anoproctosigmoidoscopy observations is contingent upon a familiarity with the normal appearance of that region. This can best be attained by frequent routine examinations. The mucosa varies normally from a deep red to salmon pink in color with the rectal portion being paler than that of the sigmoid. An injected appearing mucosa may be the direct result of too diligent measures having been taken in preparation for the examination; in that event, if there is an absence of gross bleeding in spite of gentle swabbing, mucus and/or pus, the color may be considered as within normal limits. Atrophy and hypertrophy of the mucosa in this area is similar in appearance to the same entities of mucus membranes elsewhere.

If present, the inspection should identify proctosigmoiditis, hemorrhoids, fissures, inflamed crypts, strictures, tumors, polyps, ulcers, hypertrophied papillae and congenital anomalies. Although many of our patients presented x-ray evidence of sigmoid diverticulosis, we have but rarely been able to bring into view the mouths of the diverticulae on sigmoidoscopy. In the series here reported we have been unable to demonstrate a single case of uncomplicated sigmoiditis; all of these cases were apparently eventuated or associated with one or more of the aforementioned lesions. However, chronic sigmoiditis although usually not diagnosed early is a common clinical entity (9).

Specific descriptions of ulcer types are recorded

(10-11). Nevertheless, it is preferable to corroborate the impression gained on inspection with the history, laboratory data and therapeutic tests before reaching a final diagnosis.

The ulcers of malignant lesions are as a rule deep, large and single. The ulcer edges are friable. The surrounding mucosa usually presents slight or no inflammatory changes. Ulcers of tuberculous origin are more apt to be irregular, deep and large. The edges are indurated and undermined. Tuberculous ulcers do not tend to confluency and the intervening mucosa is reasonably normal in appearance. Amebic ulcers likewise are discrete and separated by fairly normal appearing mucosa. The walls of an amebic ulcer are edematous with the ulcerated areas being oval or round and small. Being friable they bleed easily. Chronic bacterial ulcerative colitis presents evidence of a stripping of the mucosa with a proctosigmoiditis. The ulcers tend to confluency so that there is a relative variation in size depending upon the degree of confluency that has taken place between them. There may be scattered areas of small scars indicating that some of the ulcers had healed. Beyond these variations they closely resemble the amebic variety.

Tumors of the rectosigmoid are still too frequently overlooked until late symptoms have developed. Proctosigmoidoscopy will invariably bring into view an existent neoplasm. Serious errors may result by depending entirely on colon enema x-ray study. Small lesions of the rectosigmoid are too frequently overshadowed by the barium solution. Further, thereby finding a lesion in the colon does not exclude the possibility of an existing lesion lower down. One of us (A.X.R.) recently observed in private practice a small polypoid sigmoidal adenocarcinoma in a patient with a partially obstructing carcinoma of the transverse colon. Reuling, Rossien and Lakes (12) reported a case of squamous cell carcinoma of the oesophagus with adenocarcinoma of the rectum. In each of these cases the lowest bowel lesions were observed on routine proctosigmoidoscopy.

TABLE IV

AGE INCIDENCE OF HEMORRHOIDS

Total number of cases studied								550
Total number having hemorrhoids								123 or 22.3%
Decade	2nd	3rd	4th	5th	6th	7th	8th	Total Percent
Females	5	17	27	19	5	2	0	75 60.9%
Males	2	8	13	12	11	2	0	48 39.1%
Total	7	25	40	31	16	4	0	123 100.0%

Neoplasms of the rectosigmoid may be benign or malignant, split-pea size to considerably larger, single or multiple and polypoid or sessiloid. While polypi may be of chronic inflammatory origin, Swinton and Warren (13) concluded from their study that rectal polypi are true tumors and not of inflammatory origin. Kennedy and Weber (14) and McKenney (15) have called attention to the familial tendency of polyposis. Malignant changes occur more frequently in polyposis than in the solitary or scattered variety. A previous report (8), of which the cases are a part of this communication, included a patient that illustrated both the familial and malignant change tendencies of polypi. The patient's brother had had a similar rectal lesion which was diagnosed and resected in another hospital. Our patient

experienced a spontaneous amputation of the tumor after biopsy tissue had been removed and studied.

It is not within the province of this presentation to discuss at length carcinoma of the rectosigmoid. This has been amply discussed by Rankin (1), Sutton and Hirshfeld (16), Gorder (17) and others. This condition is either on the increase or the medical profession at large has become alerted and therefore finds it more frequently than previously. Proctosigmoidoscopy offers the best means of early diagnosis and should be instituted on all patients, particularly those experiencing gastrointestinal symptoms or otherwise unexplained hypochromic anemia.

Rectosigmoid carcinoma is usually easily distinguishable from other tumors. The mass is annular or oval with an overgrowth of tissue suggesting the appearance of a cauliflower. It bleeds easily due to its friability. As a consequence of its friability biopsy tissue can frequently be obtained with a cotton swab. The surrounding mucosa is practically devoid of inflammatory changes. This tumor tends to ulceration. The description of malignant ulcer has been previously mentioned.

REPORT ON SERIES EXAMINED

A total of 550 unselected consecutive cases from the Queens General Hospital Gastrointestinal Clinics comprise the series herein reported. Table 1 reveals that 40.9% (225 patients) presented one or more lesions of the ano-recto-sigmoid region. Table 2 reveals that there was a total of 251 lesions encountered during the examinations and of this number 139 or 55.37% were asymptomatic. It was our experience to observe that frequently patients are prone to be reluctant about volunteering information pertaining to the anorectal region except when the symptoms are quite troublesome. In consequence, when progressing to that part of the routine history, we first make inquiry relative to the presence of blood in or on the feces. This inquiry is of sufficient significance to the patient to invariably result in a positive or negative reply. The path is thereby usually cleared for further interrogation.

Many of the observed lesions were noted without the use of the proctosigmoidoscope. It is noteworthy, as Table 2 indicates, that the addition of this instrument to the armamentarium had greatly increased our diagnostic capacity. The major portion of carcinomatae of the rectosigmoid are within the reach of this instrument. W. J. Mayo is quoted (18) as stating that in a series of 100 consecutive cases of carcinoma of the rectum and rectosigmoid 63 were located in the rectosigmoid region. Obviously these could not have been brought into direct view without the aid of the proctosigmoidoscope.

It will be noted in Table 2 of the 19 cases with polypoid six were malignant, of which three were asymptomatic. In 57.89% of the polypoid cases there were no symptoms. The overall number of malignancies in the 550 cases routinely proctosigmoidoscoped was eleven (.2%). Of these eleven malignancies 36.36% (four) were asymptomatic.

Patients having sigmoiditis, proctitis, proctosigmoiditis, fistula-in-ano, fissure, anal ulcer and chronic ulcerative colitis would generally be expected to have symptoms attributable to these conditions. It is noteworthy that 12 patients in whom these lesions were observed

were asymptomatic and 17 had symptoms. One can only hypothesize as to the number of these patients that might have had subsequent malignant changes.

Table 3 reveals that ano-recto-sigmoid disease is most frequent in the third, fourth, fifth and sixth decades in both sexes. Further, the incidence of these lesions was 10.2% greater in females than in males. This higher incidence could probably be explained on the basis of childbearing, mode of life and differences in the anatomy of the pelvic contents.

It will be noted in Table 4 that 22.3% of the 550 patients studied had hemorrhoids. Further, the incidence of hemorrhoids was 49% of the total number of the 251 lesions observed in the 225 patients having ano-recto-sigmoid disease. In this series hemorrhoids were 21.8% more frequent in females than in males. The ratio in the fourth decade was slightly more than 2:1 in favor of the females.

CONCLUSIONS AND SUMMARY

The purpose of this presentation is to further propound the importance of routine proctosigmoidoscopy. A discussion of the preparation of the patient, precautions, technique, observations and a report on 550 unselected consecutive cases is included.

A procedure that reveals 251 lesions in 225 patients of a series of 550 cases must certainly be utilized routinely in every gastrointestinal study. In deference to the multiplicity of the trials and tribulations of the general medical practitioner proctoscopy is a minimal requirement. The fact that 55.37% of the lesions herein cited were asymptomatic gives further precedence to these contentions.

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SWALLOWED INTESTINAL DECOMPRESSION TUBES

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THE ACCEPTANCE of the intestinal decompression tube as an effective instrument for the treatment of intestinal distention has resulted in its widespread use. It was only inevitable that errors as well as accidents would occur in the use of this instrument. One accident, which is usually harmless but has been considered as being dangerous, is the swallowing of the entire intestinal tube by the patient. This accident can occur in many different ways: (1) The patient may deliberately swallow the intestinal tube (2) the interne or nurse may permit the intestinal tube to be swallowed as a means of removal, (3) it may be difficult or impossible to remove the tube from the nose and hence the tube may be permitted to pass downward for excretion per rectum, and (4) When an intestinal tube is not fastened to the face of the patient, on occasion peristaltic activity may be so forceful that the tube emerges from the anus. When this happens, it is permitted to be swallowed and is best removed from below.

The patient may deliberately swallow the intestinal decompression tube to satisfy some mental aberration. Such patients are in the same group as those that swallow coins, pins, hairpins, and a wide variety of foreign bodies. In such cases, if there is no evidence of obstruction to the intestinal stream the tube will invariably pass through and be excreted per anus just as any other foreign body. The length of time needed for this to occur is extremely variable. It depends upon the peristaltic activity and tonus of the bowel as well as the presence or absence of kinks or angulations in the bowel due to adhesions which may cause a partial intestinal obstruction. In this latter event, the downward passage of the intestinal tube would be blocked at the level of the partial obstruction. The failure of a tube to be excreted in a reasonable period of time need not necessitate surgical intervention in the absence of signs of bowel obstruction. As short a time as four hours and as long a time as eighteen days may elapse between the time the tube was swallowed and the time it is excreted per rectum without any harm whatever to the patient. In well over 5000 intubations at Grace Hospital during the past seven years, the shortest period of time required for a tube to be excreted after being swallowed was four hours (see fig. No. 1) and the longest period of time was eighteen days (see fig. No. 2). On one occasion, however, a balloon of an intestinal decompression tube slipped off and remained

within the bowel for twenty-nine days before being excreted. In no case was any harmful effect noted either by the patient or attending physician.



Fig. 1.: Note tube head at rectosigmoid.

Fig. 4: Same as figure 1.

On occasion, such tubes may fail to pass as a result of adhesions which so kink and angulate the bowel that the tube cannot pass through this narrowed segment of bowel. Failure of an intestinal decompression tube to pass per rectum when associated with an increasing or recurring intestinal distention is highly suggestive of a partial bowel obstruction being present distal to the tube. Such obstruction may be complete or partial. In either event the treatment is surgical. Releasing the obstructing process distal to the tube will invariably result in an easy passage of such tubes through the previously obstructed area and then excretion per rectum.

Grace Hospital.

Submitted March 15, 1951.

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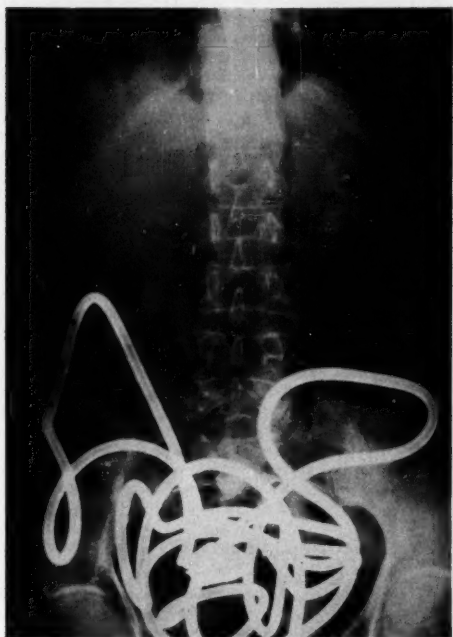


Fig. 2: Tube cut off at the nose and permitted to pass down by the interne as a method of removal. Tube excreted eighteen days later.

tum. When the obstructing process is due to adhesions, which account for most of such cases, simple lysis of the adhesive bands is usually sufficient. Enterotomy to remove the tube is not required and needlessly exposes the patient to peritoneal soiling. The same surgical principle applies to such cases as would apply in the absence of a foreign body within the bowel. Whenever the circulation of the bowel is impaired so that a question of viability arises, resection of the bowel would be indicated. In this event, removal of the tube could be done without increasing the risk. In the vast majority of cases, however, there is no circulatory impairment so that simple lysis of the adhesions is all that is required.

The following case report is a good example of an uncomplicated case in which an intestinal decompression tube was swallowed by the patient deliberately.

CASE REPORT

E. M., age 50, male, white was admitted to the hospital May 31, 1950, complaining of upper abdominal pain, vomiting and distention. He had been well until three days ago when he was seized by severe upper abdominal pain and vomited three times. The vomitus was green and slimy. Although the abdominal pain and distention persisted he did not vomit after the first day. On examination he was found to be an adult male who lay in bed very apprehensively. He seemed to be in much pain. The only positive physical findings were limited to his abdomen which was distended. It was quite tender over the entire hypogastric region and to the right of the umbilicus. His lower abdomen was not tender on palpation. No rigidity. His temperature was 98, pulse 84, and respirations 22 on ad-

mission. On June 1, 1950 the abdominal distention had increased. Several enemata were ineffectual. On June 2, 1950 a Cantor tube was passed. After it passed through the pylorus, prostigmin was given in a dose of one ampoule every 4 hours for four doses. On June 3, 1950 the Cantor tube was found to be far down the gastrointestinal tract and the distention was considerably alleviated. Radiological studies on June 5, 1950 showed considerable improvement in the small bowel distention with the head of the Cantor tube in the ileum. It also disclosed that a Cantor tube had been passed on the night of admission and had been torn out by the patient leaving the mercury filled balloon in the bowel. On June 7, 1950 the continuous suction was disconnected. Thereupon the patient proceeded to swallow the intestinal decompression tube (See fig. 3). On June 9, 1950 an enema was effectual for feces. The mercury filled balloon of the first tube was excreted intact (1). This had been in the bowel for ten days. His condition remained good. On June 11, 1950, he had a normal bowel movement and excreted the entire Cantor tube that he had swallowed intact. This tube had remained in the bowel for four days asymptotically.

Hanselman and Theis (2) reported a case of this type in which surgical removal of a Miller-Abbott tube was required through a minimal enterotomy. In this case, three sharp kinks were found in the bowel distal to the tube as a result of adhesive bands.

The interne, nurse, or resident may permit the intestinal tube to be swallowed by the patient as a means of removal. This is particularly apt to occur when an uninitiated nurse or interne is called to remove a tube which has passed far down the gastrointestinal tract. On several occasions the nurse considered it easier for the patient to pass the tube per rectum rather than removing it from above. In each case, the tube was permitted to be swallowed by the patient. The following case report is an example of this type of case:

CASE REPORT

A. B., age 40, white, female was admitted to the hospital March 2, 1950 for salpingectomy. At operation, a right salpingo-oophorectomy and appendectomy was done. She had an uneventful recovery and was discharged on March 8, 1950. She was re-admitted to the hospital on April 5, 1950 with a draining sinus in the lower portion of the abdominal incision. A purulent feculent material oozed from this sinus. A Cantor tube was passed on April 6, 1950. The tube passed rapidly down the gastrointestinal tract. Continuous suction was applied to the tube and large doses of antibiotic given. As a result, the drainage from the sinus ceased on April 11, 1950. The surgeon in attendance ordered the tube removed on April 15, 1950. The nurse disconnected the tube from the suction and permitted it to be swallowed because she said, "It seemed easier that way since the tube was so far down." A flat plate of the abdomen on April 15, 1950 showed the intestinal tube to be at the rectosigmoid. This film (See fig. 4) was taken at 10:00 a.m. At 1:00 p.m. (noon) an a.s. enema was given. This was very effective for stool. The Cantor tube was expelled per anus intact at this time with the stool.

It may be difficult or impossible to remove the tube from above. This may be caused by two widely different conditions. First, it may occur as a result of sphincteric unrelenting spasm in a nervous highly apprehensive individual. Secondly, it may occur as a result of the permeation of intestinal gases within the balloon of the intestinal tube. In this latter event the balloon becomes so large that its removal from above is very difficult or even impossible at times.

In cases in which it is difficult to remove the tube from above, the tube may be deliberately permitted to pass downward for excretion per rectum. The nervous, apprehensive, high strung individual may become so disturbed when one attempts to remove the intestinal tube from above that severe and persistent sphincteric

spasm occurs which effectively traps the tube within the bowel. In such cases, giving sodium luminal and atropine by injection may so relax the patient that removal from above may be possible with ease. On one occasion, despite this procedure it was impossible to remove the intestinal tube from above. The tube was then cut off at the nose and permitted to be excreted per rectum. The details of this case are as follows:

CASE REPORT

H. P., a fifty year old colored man was admitted to the hospital with a diagnosis of malignant hypertension and uremia. His N.P.N. was 88 on admission. An attempt to treat this uremia by intestinal dialysis was thought worth attempting. The patient although extremely nervous and apprehensive consented to this. After sedation and considerable coercion, an 18 fr. Cantor tube was passed. This tube moved down the gastrointestinal tract rapidly so that a twenty-four hour film demonstrated the tube head in the ileum. This tube was then fastened to the nose. A second Cantor tube of 12 fr. diameter was then passed through the other nostril. This second tube also was pulled back so that the tube head would come to lie in the upper jejunum. Continuous suction was then applied to the 18 fr. tube in the ileum and saline permitted to drip into the bowel through the 12 fr. tube in the upper jejunum. As a result of this, the N.P.N. dropped to 40 in two days. At the end of one week's treatment, the patient refused to co-operate further and insisted that the tubes be removed. Upon attempting to do so, it was found that the tubes came out freely for the first two feet and then became arrested. It was impossible to remove them. The patient would become rigid and would tighten his skeletal muscles upon attempting to do so. The tubes were both cut off at the nose. The 12 fr. tube was excreted per rectum on the fifth day thereafter, and the 18 fr. tube was excreted on the 8th day. (See fig. 5).

As a second cause for one's inability to remove a tube from above, the balloon may be found to be so filled

with intestinal gases that the bulk of the tube head makes removal from above difficult if not impossible. (3,4,5) This is apt to occur most often with the Harris tube because the balloon of this tube is six inches long and may take up as much as 125 c.c. of gas. Harris (6) has noted this occurrence and advised permitting the tube to be excreted per rectum. This usually occurred in the absence of bowel obstruction distal to the tube head because the intestinal gases diffuse out of the balloons when the circumjacent bowel has been decompressed. If the bowel distal to the balloon is kinked, angulated, narrowed or the site of an intestinal anastomosis, it may be necessary to operate upon the patient before the tube can be removed. In the absence of signs or symptoms of bowel obstruction this should not be done, conservatism and watchful waiting will often be rewarded by the ultimate passage of the tube. The development of signs of bowel obstruction in such cases is an absolute indication for immediate operation. In this event, simply squeezing the distended bowel about the balloon between the palms of the surgeon's hands causes the balloon to break. This then permits the tube to be simply removed via minimal enterotomy or if the obstructing process has been released such tubes will readily be excreted per rectum. In no event should the tube be removed with the inflated balloon. To do so would necessitate an unnecessarily long enterotomy incision. If the tube had not been swallowed by the patient, after collapse of the gas filled balloon, the tube may readily be removed from above.

There have been case reports of intussusception of

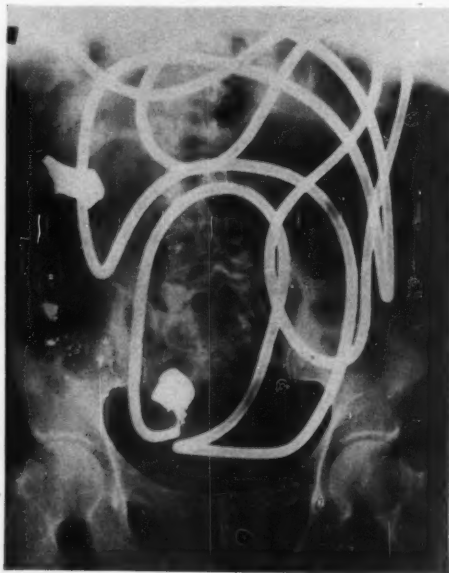


Fig. 3: Note loose mercury filled balloon in the ascending colon. This was excreted nine days after being lost in the bowel. The tube itself was then excreted four days after being swallowed.



Fig. 5: Film taken with bedside unit and hence poor quality of film. Note the presence of two intestinal tubes. One tube of 18 fr. diameter and one of 12 fr. diameter. These were excreted on the eighth and fifth days respectively.

the jejunum or ileum as a result of the presence of an inflated Miller-Abbott tube (7,8,9). In such cases, the inflated balloon acts much like a space occupying tumor and furnished the nidus for the intussusception. Removal of the tube may then be impossible from above. In any event, surgical correction of the intussusception is imperative in such cases.

In some patients, the peristaltic activity may be so active that the tube head may be found to have emerged per rectum. In cases of this type, the need for intubation no longer exists. For aesthetic reasons, such tubes are released at the nose and pulled out per rectum. As an example of this type we find the following case report: (See fig. No. 6).

CASE REPORT

A. K., a seventy year old white woman was admitted to the hospital for a resection of the right colon. This was done. Following operation, she developed a progressively increasing intestinal distention with vigorous peristalsis. It was thought that a partial obstruction had occurred at the anastomotic site due to edema. A Cantor tube was passed. Forty-eight hours later the tube head was found to have emerged from the anus and lay free in bed. The tube was removed from below.

SUMMARY

Intestinal decompression tubes may be swallowed by patients for various reasons. In general, one may classify such cases into four main groups: (1) Group one—patient may swallow the intestinal decompression tube to satisfy some mental aberration, (2) Group two—patient may swallow intestinal decompression tube because the interne or nurse instructed patient to do

so in order to remove the tube, (3) Group-three —It may be difficult or impossible to remove the intestinal tube from above. In such cases the tube may be cut off at the nose and permitted to pass per rectum. In this group, three main causes are found: (1) persistent spasm of sphincters as found on attempting to remove a tube from a nervous, apprehensive, high strung individual, (2) Permeation of intestinal gases into the balloon of the intestinal tube. Such balloons may become so bulky that it is difficult or impossible to remove them from above, (3) An air filled balloon of an intestinal decompression tube may behave like a space occupying tumor within the bowel and produce intussusception. The fourth group of patients consists of those individuals in whom peristaltic activity is so active that the intestinal tube is found to emerge from the anus.

The treatment of patients in whom an intestinal decompression tube has passed down the gastrointestinal tract is essentially the same as the treatment for any other foreign body within the bowel. In the vast majority of cases such tubes will be excreted per rectum. The length of time required for this to occur is variable. It may be as short a time as four hours, or it may require eighteen days. Patience on the part of the attending physician and re-assurance of the patient is all that is required. Any intestinal decompression tube that does not ultimately pass per rectum or becomes arrested along the gastrointestinal tract, is presumptive evidence of partial bowel obstruction distal to the end of the tube. An occasional case will become arrested because of marked inflation of the balloon by gas which cannot pass through a kinked or angulated bowel which would normally permit the free passage of intestinal contents. In such cases, surgical correction of the partial obstructing process will permit the tube to be passed uneventfully. If the abdomen is opened and a markedly distended bowel about a gas filled balloon is found, compression of the balloon between the palms of the surgeon's hands easily breaks the balloon permitting its removal via a minimal enterotomy. The treatment of intussusception caused by the space occupying property of an air filled intestinal tube is purely surgical, and that as soon as possible.

CONCLUSIONS

- (1) An intestinal decompression tube swallowed by patient will usually pass through the gastrointestinal tract in the absence of obstruction.
- (2) The length of time required for a swallowed tube to be excreted varies from four hours to as long as eighteen days.
- (3) Failure of a tube to be excreted per rectum does not in itself constitute an indication for surgical intervention.
- (4) Failure of a tube to be excreted in a reasonable length of time associated with intestinal distention, obstipation, pain, and vomiting (bowel obstruction) is a definite indication for surgical intervention.
- (5) Intussusception caused by an air filled balloon of an intestinal tube constitutes a positive indication for immediate surgery.

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Fig. 6: Tube spontaneously passed per rectum forty-eight hours after intubation as a result of vigorous peristaltic activity.

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GASTRIC SURGERY IN THE AGED

ROLAND P. REYNOLDS, M.D., F.A.C.S. AND MEYER O. CANTOR, M.D., F.A.C.S. Detroit, Mich.

The increase in life expectancy in this era has brought with it problems of medical care. From this need arose the relatively new specialty of geriatrics. One might suspect from this that the aged required a type of treatment completely different than the younger age group. This in fact has been the case with some types of major surgery in the aged. For many years surgeons would attempt gastric operations upon the aged only with great reluctance because of the almost prohibitive mortality rate.

With the advent of early ambulation after operation as a means of restoring the deranged physiology to normal in as short a time as possible, it was soon noted that aged patients were particularly benefited. Hypostatic pneumonia was very common following major surgical procedures prior to the advent of early ambulation, but has been reduced to a very low level in recent years.

The improvements in surgical technic and our increased knowledge of water and electrolyte metabolism, with the liberal use of the antibiotics, has made it possible to perform the most extensive operations in the aged without prohibitively increasing the mortality rate.

Between the years of 1943 through 1947, four hundred and eighteen gastrectomies were performed at the Grace Hospital with an overall mortality rate of 10%. These operations were performed by all surgeons having major surgical privileges.

During this same period of time, seventy-four of the four hundred and eighteen patients were over the age of sixty. The oldest patient having a gastrectomy was eighty-six years old. It is thus evident that 17.7% of all patients subjected to gastric surgery were over the age of sixty.

The mortality rate for this group of seventy-four patients over the age of sixty was 16.2%. Comparing this figure with that for gastric surgery at all ages one notes that although the mortality rate has increased by 6.2%, this does not constitute a prohibitive increase. The fact that a patient was well over sixty or even seventy years old need no longer be a deterrent to gastric surgery when indicated. Such surgery in this age group, just as in the younger age groups, was undertaken only after the patient had been well worked up and the indications for surgical intervention unmistakable. Gastric carcinoma and elective surgery for duo-

denal ulcerative lesions were the most important indications for surgery in this age group. In general the indications for surgery in this age group were the same as in the younger age groups with the exception of the treatment of gastroduodenal hemorrhage. In the younger age groups, one massive hemorrhage was not considered an indication for gastrectomy. In the age group above sixty, however, patients who had one massive gastroduodenal hemorrhage were considered candidates for gastrectomy, the difference in our indications being dependent upon the sclerosis of the main arteries of the stomach found after the age of sixty. Such sclerotic vessels we believe more likely to exsanguinate the patient in the event of erosion. The results of surgery for this indication were uniformly good.

In reviewing the list of patients in this group of seventy-four, it was found that fifty-eight patients (79%) were between the ages of sixty to seventy years old. In the seventy to eighty year old group, eighteen patients were operated upon for an incidence of 18%. Two of the patients were between the ages of eighty to ninety years old, an incidence of 2.7%. It should be apparent that although the majority of the patients operated upon were below the age of seventy (79%), nevertheless 18% of the patients were seventy years old or older. In this latter group, in former years only surgery of the most conservative type would have been undertaken.

The indications for surgery and the pathological findings at operation showed some difference between this older group of patients as compared with the group of patients under the age of sixty. Forty-two patients (56%) were operated upon for duodenal ulcerations. Most of these patients had a history of one or more massive hemorrhages. Eleven patients (14%) were operated upon for gastric ulcer. The combined percentage of patients operated upon for gastric and duodenal ulcerative lesions was 6% lower than in the younger age group. Fourteen of the patients were operated upon for carcinoma of the stomach for an incidence of 18%. This figure is higher than the 5% noted in the younger age group. These results are not surprising because of the increase in life span in which malignant lesions are commonly found. One patient, 1.3%, was operated upon for a marginal ulcer. Three patients were operated upon for chronic hypertrophic gastritis, an incidence of 4%. Two patients had gastric polyps (2.6%) and one patient

presented a herniation of the stomach through a diaphragmatic hernia (1.3%).

There were twelve deaths in this series of seventy-four patients. In reviewing the cause of death, it was found that peritonitis was responsible for eight of the twelve deaths. The second most common cause of death was post operative hemorrhage. In only one case was cardiac failure a cause of death. Both peritonitis and post operative hemorrhage are causes of death most likely due to faulty surgical technic and should be attributed to poor surgery rather than the age of the patient operated upon.

Nine of the patients in this group of twelve deaths were found to be in the sixty to seventy year old group, an incidence of 75%. Three of the patients were in the seventy to eighty year old group, an incidence of 25%. The number of patients that died in each age group were in the same ratio as the number of patients in each group in the entire series of patients operated upon. From this point of view, we note no increase in mortality rate beyond the age of seventy.

SUMMARY

In reviewing a group of seventy-four patients subjected to gastric surgery who were sixty years old or older, an overall mortality rate of 16.2% was found. Comparing this mortality rate with the 10% mortality for all gastric surgery in series of four hundred and eighteen patients operated upon between the years of 1943-1947, we see an apparent increase which would appear to be due to the older age of the patient. In re-

viewing the cause of death, however, we find that the same proportion of deaths occurred in the sixty to seventy year old group as in the seventy to eighty year old group. We note 79% of all patients operated upon in this series to be between the ages of sixty to seventy, whereas 18% of the patients were between the ages of seventy to eighty and 2.7% of the patients were over the age of eighty. In studying the causes of death, 75% of all deaths occurred in the sixty to seventy year old group and 25% of the deaths were found in the seventy to eighty year old group. From these figures, it should be obvious that the age of the patient alone had nothing to do with the death of the patient.

A scrutiny of the causes of death again reveals the startling fact that only one patient died of cardiac failure. This might conceivably be attributed to the age of the patient, yet this patient was only sixty four years old. Eight of the patients died of peritonitis (66%) and three of the patients died of post operative hemorrhage (25%). Since both of these causes may more rightly be attributed to faulty surgical technic, we must conclude that 91% of all deaths in this older age group were not the result of the age of the patient per se.

CONCLUSIONS.

1. The age of the patient does not appreciably increase the mortality rate for gastric surgery.
2. Peritonitis and post operative hemorrhage were responsible for 91% of all deaths in the patients operated upon beyond the age of sixty.
3. Neither of these causes are in any way influenced by the age of the patient.

ABSTRACTS ON NUTRITION

FOY, H., KONDI, A. AND HARGREAVES, A.: *The response of megaloblastic macrocytic anemia to crystalline penicillin G*. Brit. Med. J., Feb. 24, 1951, 380-383.

A case of very severe, macrocytic, megaloblastic anemia in a native woman in Kenya, responded to the administration of 400,000 units of crystalline penicillin G daily for 7 days. Her reticulocytes rose to 37% and this was followed by a rise in the hemoglobin and red blood cells. No other treatment was given. In many ways the case appeared to be one of pernicious anemia. The response to penicillin did not differ in any way from that obtained from potent liver extract, folic acid, B₁₂ or marmite. Some organism competing for hemopoietic substances may have been destroyed. Some hemopoietic antagonist may have been destroyed. Other possible explanations are advanced. The authors are continuing the treatment of native megaloblastic anemias with penicillin alone.

LAWRENCE, R. D.: *Types of human diabetes*. Brit. Med. J., Feb. 24, 1951, 373-375.

The term "diabetes mellitus" includes a variety of glycosuric conditions separate both in clinical type and in etiology. Lawrence emphasizes that there is the fat diabetic (lipoplethoric) who probably has no deficiency in insulin and whose glycosuria can be controlled by loss of weight. These patients do not develop ketosis or coma. Then there is the usual diabetic who certainly is insulin-deficient and who, in the absence of insulin treatment, is prone to develop ketosis rapidly. He describes a third and very rare type of diabetic who lacks the ability to deposit fat anywhere in the body and who is insulin resistant. He uses the term "lipotrophic" to designate this rare type. Studies with labelled glucose in tracer experiments indicate that insulin turns glucose into glycogen, but almost

equally rapidly, into stored fat. Acting on a large meal, insulin is quantitatively more lipogenic than glycolytic.

KENNEDY, R. J. AND KRICHBAUM, F. M.: *Ocular fundus findings in 133 cases of diabetes mellitus*. Cleveland Clinic Quart., 18, 2, Apr. 1951, 134-140.

133 cases of diabetes of various duration were divided into those with systolic blood pressure over 160 and those with systolic pressure under 160. The former group showed retinal hemorrhage in 62.4 percent, the latter in 56.1 percent. Retinal hemorrhages in the absence of exudates were unaffected by the presence of hypertension. Hemorrhages increase in frequency with age, with hypertension, and with duration of the diabetes. Intravitreal hemorrhage, retinitis proliferans and glaucoma were relatively infrequent findings. Cataract was present in 38.3 percent of the cases studied.

FRANCIS, C.: *Research and development in the food processing industry*. Nutrition Reviews, 9, 3, Mar. 1951, 65-67.

Clarence Francis, Chairman, General Foods Corporation, and a Trustee of the Nutrition Foundation, Inc., in addressing the Industrial College of the Armed Forces, stressed the indispensability of research in the food processing industry, and felt that the scope for advancement in this field was so enormous as almost to leave one in a state of "fascinated paralysis." Research made possible frozen foods. It was able to capture the flavors in Jell-O, produce precooked rice, decaffeinated coffee, and now faces tremendous possibilities through the utilization of electronics. The production antioxidants, emulsifiers, vitamin fortifiers, better methods of packaging, are but a few of the 4500 topics now being examined

by 650 research laboratories. More effective relationships between industry and the Quartermaster Food and Container Institute are evolving through the operation of The Associates Food and Container Industry. War conditions tend to speed up the perfecting of methods used by the food processing industries.

HILBRETH, E. A., MELLINKOFF, S. M., BLAIR, G. W., AND HILBRETH, D. M.: *The effect of vegetable fat ingestion on human serum cholesterol concentration*. *Circulation*, 111, 5, 641-646, May 1951.

The following results were obtained in a study designed to show the effect on serum cholesterol when vegetable fat containing no cholesterol was added to a diet in which total fat had previously been restricted. 1. In 3 healthy male physicians a reduction in the dietary fat produced a significant fall in the serum cholesterol concentration. 2. In 2 of the individuals, addition of vegetable fat to the diet was associated with a rapid rise in the serum cholesterol to the levels observed before fat restriction. In the third, the serum cholesterol rose much more gradually, but also attained the control values. 3. It would therefore seem that in these 3 subjects the restriction of total fat and not of cholesterol alone was probably the decisive factor in lowering the serum cholesterol concentration.

PYKE, M.: *Industrial nutrition*. *Nutrition Reviews*, 9, 4, 97-100, April 1951.

Magnus Pike, of the Yeast Research Outstation, The Distillers Co., Ltd., Glenochil, Clackmannanshire, Scotland, indicates that feeding the industrial worker is a most complex problem requiring knowledge of nutrition, physiology and sociology. Average requirements in calories and nutrients must be the basis of the undertaking although important variables come into the problem. Peculiar or traditional diets ought not to be condemned until their nutritional composition is known. The modern tendency in industry is to lighten the demands for heavy physical work because mechanical help is so much cheaper. The majority of workers eat more than three meals a day, and the timing of these meals is important, for it is now believed that frequent feeding is salutary, and increases muscular efficiency. Food must be acceptable, or it is not eaten. The canteen must take into consideration what the worker eats at home and attempt to supply the lacking nutrients. The human element in industrial nutrition requires more emphasis.

BARNETT, A. J.: *Blood flow in gout*. *Brit. Med. J.*, Apr. 7, 1951, 734-6.

Measurement of the blood flow during an attack of acute gout showed that the resting flow in the foot of the limb less affected by peripheral vascular disease was very high and little increased by reactive hyperemia. In the foot of the other limb, which was more affected by peripheral occlusive vascular disease, the resting blood flow was in the range of high normal values both during the attack of acute gout and when it had almost subsided. The demonstration of the high blood flow in acute gout lends strong support to the thesis of Prof. Wood Jones that the basis of this condition is a vasomotor disturbance akin to erythromelalgia. The agent causing the syndrome of acute gout would seem to be one of the most powerful peripheral vasodilators known, but even if it were isolated, one would hesitate to give it a therapeutic trial in view of the suffering it might give rise to.

CLELAND, J. B.: *Biochemical aids in the diagnosis of deficiency of the vitamin B complex*. *Med. J. Australia*, 1, 13, Mar. 31, 1951, 468-476.

Simple methods of estimating the thiamine, riboflavin and methylnicotinamide content of the urine are described, and

normal values given. Statistical analysis has shown that people with hypertension, peripheral neuritis, alcoholism, cirrhosis or cancer of the liver, congestive cardiac failure, symptoms of deficiency diseases or history of malnutrition, or gastro-intestinal disturbances are likely to have a low thiamine excretion. Those with hypertension, peripheral neuritis, alcoholism, malnutrition, or G. I. disturbances are likely to have a low excretion of methylnicotinamide. Reduced riboflavin excretion is usually associated with a low thiamine excretion.

CLEMENTS, F. W.: *Infant foods*. *Nutrition Reviews*, 9, 5, May 1951, 129-131.

Clements, of the World Health Organization, Geneva, traces the rapid growth of the use of cow's milk in infant feeding during the present century and notes a marked drop in infant mortality from gastroenteritis and other diseases as well. This improvement in North America and Europe naturally followed the development of the dairy industry. He contrasts this happy state with most Asiatic and African localities where milk is practically unavailable and where infant mortality remains high. The only practical solution of this wide-spread difficulty is to find good milk substitutes, made from indigenous cereals and fruits. While this has already been accomplished on a small scale, it will require time to bring Western-trained pediatricists to accept such formulae.

BORNSTEIN, J. AND LAWRENCE, R. D.: *Two types of diabetes mellitus with and without available plasma insulin*. *Brit. Med. J.*, Apr. 7, 1951, 732.

In alloxan-diabetic hypophysectomized and adrenalectomized rats, the blood sugar levels are sensitive to very small amounts of insulin, e. g., 1/20,000 of a unit of insulin (0.05 millunits). The injection into such rats of 1 ml. of plasma taken from a diabetic person 2 hours after the oral ingestion of 50 g. of glucose, will show whether or not any insulin was present in the blood of the patient. By such means, the authors differentiated two types of diabetes. The first type is generally young and characterized by hyperglycemia, rapidly developing ketosis and severe weight loss and by the need of insulin to live. The second type consists largely of middle-aged obese females with similar grades of hyperglycemia and glycosuria but with no ketosis and no important loss of weight. Their diabetes is easily controlled by low diets without insulin, particularly if weight is reduced. This finding opens wide possibilities for research into the nature and cause of diabetes.

CACHERA, R., LAMOTTE, M. AND LAMOTTE-BARRILLON, S.: *Confrontations anatomico-cliniques et biologiques concernant le foie dans l'alcoolisme chronique*. *Bull. L'assn. d'études physio-pathologiques du foie et de la nutrition*. No. 13, 1950, 20-79.

In 82 alcoholic subjects, the state of the liver was followed by serial punch-biopsies and compared with the clinical findings and functional studies. A tremendous fatty infiltration of the liver without clinical signs of cirrhosis was the dominant anatomical characteristic of alcoholic hepatitis. The disappearance of the fatty infiltration is favored by dietary treatment and lipotropic drugs. Serial biopsies showed the relationship between fatty infiltration and the evolution of cirrhosis. The liver plays an important role in the synthesis of phospholipids. The fatty liver in alcoholics is an infiltration, not a fatty degeneration and is due to failure in the synthesis of phospholipids. In alcoholics the irregularities of diet rather than the alcohol itself probably explain the disease, because it can result from purely nutritional disturbances and because so little is known for certain about the direct effects of alcohol on the liver. The endocrines, upset by chronic alcoholism, may play a part in mobilizing the fatty reserves of the tissues and transporting them to the liver. The authors examine the relationships between fatty infiltration and cellular necrosis in the liver.

BOOK REVIEWS

ROENTGEN MANIFESTATIONS OF PANCREATIC DISEASE. Maxwell Herbert Poppel, M. D., F. A. C. R., 389 pages, Charles C. Thomas, Springfield, Ill., 1951, \$10.50.

It is difficult to offer a brief review of this book, because it must be studied in detail to gain a full appreciation of its value. Dr. Poppel has approached what is regarded as perhaps the most difficult problem in gastro-enterologic x-ray very methodically and illustrated his text with a profusion of beautifully reproduced half-tone engravings of x-ray films. Naturally the whole upper abdomen comes into review and consideration. On finishing the volume, the physician will feel that the x-ray diagnosis of pancreatic diseases is not nearly so obscure and difficult as he had imagined. Every physician reading x-ray films should obtain the book.

MODERN DIETETICS. Doris Johnson, B. S., M. S. Edited by Hazel E. Munsell, Ph.D., 529 pages, G. P. Putnam's Sons, New York, 1951, \$4.95.

In emphasizing her favorite theme—that all special diets should be built around the normal diet—Miss Johnson has presented the nursing and medical profession with an entirely new book embodying all the various phases of progress which have been made in the past two decades. Normal nutrition is first dealt with and then the dietary treatment of disease is taken up. Cookery is by no means neglected. A "Questions and Problems" section of each chapter epitomizes the work as one reads it. Many valuable tables are added. We highly recommend the book to all physicians and nurses.

DISEASES IN OLD AGE. Robert T. Monroe, M. D., 407 pages. Harvard University Press, Cambridge, June 7, 1951, \$5.00.

This volume represents a clinical and pathological study of all the 7,941 individuals over 61 years of age who were admitted to the medical service of the Peter Bent Brigham Hospital in Boston in the 30 years following its opening in March 1913. All physicians will find the book highly informative inasmuch as it presents a rational background for the practice of geriatrics. Monroe's chief feeling is that the old person should be approached with sympathy and care taken to apprehend his total condition, and not just one specific condition forming his chief complaint.

LE FOIE DIABETIQUE. Jacques Mirouze, M. D. L'Expansion Scientifique Française, Editors, 368 pages, 23 rue du Cherche-Midi, Paris 6E, C. C. P. Paris, 370-70, 1,300 fr.

This complex work covers all the endocrine experiments, both human and animal, done in diabetes, as well as giving a detailed interpretation of the general symptomatology, metabolic disturbances, the functional changes and the hepatic histology. The author reviews the pancreatic, pituitary, suprarenal, and thyroid aspects of the entire problem. The various procedures for investigating liver function are outlined. The original portion of the work deals with punch biopsies, and the author enters the problems of the steroid chemistry of the liver and describes a little-known vacuolar lesion, and goes on to describe the pathogenesis of the disease and the complex problems of diabetic coma and insulin resistance. Above all, he provides an original emphasis on the role of the liver in diabetes.

PAPERS DEDICATED TO PROFESSOR MARTIN ODIN ON HIS SIXTIETH BIRTHDAY (JUNE 13, 1950). Gumperts Forlag, Gøteborg, 1950.

Several of the papers in this collection deal with gastrointestinal subjects. A. Doscherholmen, J. Marcussen and O. Romeke find that in examining 30 cases of small gastric ulcers

and 17 large gastric ulcers for acidity, the gastric activity as expressed in acidity units may be lower in large than in small ulcers. S. Johnsson, H. Lindholm and Th. Stenstrom conducted a clinical and x-ray examination on 176 patients who had previously received medical treatment for gastric ulcer during the period 1930-1945. Favorable results were obtained from medical treatment in 48.1 percent, unfavorable in 51.9 percent. The longer the history of illness, the poorer was the result of treatment. No less than 11.4 percent turned out to be gastric cancer. Possibly surgery should be done on all cases who relapse on medical treatment.

Haqvín Malmros studied the effects of war on arteriosclerosis, cardiosclerosis, tuberculosis and diabetes from the standpoint of nutrition. Starvation caused tuberculosis to increase in Germany but in Norway the moderately reduced caloric supply did not lead to increased T. B. morbidity where conditions were otherwise favorable. Deaths from arteriosclerosis and cardiosclerosis in Finland declined during the "lean" years, due to reduction in cholesterol foods such as eggs and butter. In Sweden the death rate from diabetes decreased due to reduced food supplies. He feels that in Denmark, Sweden and the U.S.A., the consumption of eggs, butter, milk and other animal fats is at present too high and may involve serious risks to public health.

J. Martensson and E. Palm studied the ocular findings in 163 cases of diabetes mellitus of at least 15 years' duration. Forty percent showed normal conditions. Cataract was present in 40 percent. In 40 percent diabetic retinopathy was found with 6 cases of proliferative retinitis.

E. Norinder reports a case of post-gastrectomy hypoglycemia simulating insulinoma in whom a biopsy of the pancreas was normal.

NUTRITION AND CHEMICAL GROWTH IN CHILDHOOD. VOL. III. CALCULATED DATA. Ice G. Macy, Ph.D., Sc. D., pages 1463 to 2174. Chas. C. Thomas, Springfield, Ill., \$2.00.

This is the "most book" for two dollars ever seen by the reviewer. It contains a veritable wealth of tables providing daily averages for the intake, absorption and retention, converted to kilograms of body weight, centimeters of recumbent length and square meters of body area, and covers the trinary foodstuffs as well as minerals. Means and standard deviations are calculated. It is an excellent reference work for all nutritionists and biochemists as well as pediatricians.

CONFRONTATIONS RADIO-ANATOMO-CLINIQUES. VOLUME IV. 68 pages with 127 cuts. Edited by M. Chiray, R. A. Gutmann and J. Seneque. Masson et Cie, Paris, France.

This is the fourth volume of its kind. Cases are briefly described and x-ray films are produced before and after operation. The method is highly instructive and most of the cases are gastro-intestinal. Seldom does one encounter such beautiful half-tone reproductions.

YOUR WEIGHT AND YOUR LIFE. Alfred L. George, M. D., 272 pages. W. W. Norton & Company, Inc., New York, N. Y., 1951, \$2.95.

George believes overweight is due to eating too much, despite the protestations of fat persons to the contrary. Fat persons burn up more calories than thin persons and require more food. "The only glands concerned with the production of obesity are the salivary glands." The underlying cause of overeating is psychological. Restricting calories is the only safe and effective way to lose weight. Specimen diets are provided to show how a fat person can eat and still lose weight. The book is written for popular consumption and appears to be sound and reliable.

GENERAL ABSTRACTS

KOSEALKA, M. F.: *Multiple bee stings with hemoglobinuria and recovery.* (Bull. U. S. Army Med. Dept., March 1949, Vol. IX, No. 3).

The author describes the case of an officer stationed in Hawaii who suffered multiple bee stings of all exposed parts of the body, with severe edema, hemoglobinuria and subsequent recovery. The severity of the injuries and reaction might have been lessened had it been possible to extract the stings immediately after their deposition into the skin, since the sting apparatus when left in the skin continues to force out contained venom by muscular action. The rapid recovery of this patient is attributed primarily to the parenteral use of calcium gluconate. Calcium salts apparently lessen the phenomenon of transudation, inhibit smooth muscle spasm, and neutralize the toxic effect of the bee venom. Its use, therefore, is suggested in the treatment of stings of bees and other insects where epinephrin has failed to effect a satisfactory response. The newer antihistaminic drugs, not available at the time, are also worthy of trial.

WILKINSON, C. F. AND FANCHER, P. S.: *The coexistence of essential familial hypercholesterolemia and thyrotoxicosis.* (Bull. U. S. Army Med. Dept., April 1949, Vol. IX, No. 4, 307-311).

A case is presented with essential familial hypercholesterolemia and thyrotoxicosis. The blood cholesterol was elevated during the time that the patient was clinically toxic; and, though it fluctuated, it was always in the abnormal range. This fluctuation seemed to be unrelated to changes in the B.M.R. This case adds additional evidence in support of the belief that at times the blood cholesterol may be of very little value and even misleading in the diagnosis of thyrotoxicosis and offers an explanation of the occasional case of thyrotoxicosis with a seemingly incompatible cholesterol.

ADLER, S.: *Factors involved in the production of flatulence.* (Harper Hosp. Bull., Jan.-Feb. 1949, Vol. 7, No. 1, 185-190).

Flatulence is taken to mean a collection of gas in the stomach or intestine in sufficient quantity to cause a sensation of fullness or pain which is relieved when the gas is expelled. Gas due to fermentation does not occur in the stomach under normal conditions. Intestinal gas varies in amount depending on air swallowed, types of food used, and the condition of the tract. 70 to 80 percent of gas in the tract is atmospheric air swallowed with food, contained in the food itself or swallowed unconsciously at other times. Diffusion of gas from blood stream will not occur in significant volume unless other gases have first accumulated. Fermentation of carbohydrates and putrefaction of proteins in conditions of stasis are common sources of intestinal gas. Normally much of the gas is taken up by the blood and excreted by the lungs. The intestinal gases are oxygen, nitrogen, methane, hydrogen sulphide, hydrogen and carbon dioxide. The amount of oxygen is negligible. Onions, milk, cream and ice cream are the foods most commonly blamed for flatulence. Impaired motor function is more important than chemical disturbances and psychic and emotional factors are prominent causes.

WOOLF, A. L. AND THOMSON, H. R.: *Spontaneous intra-abdominal hemorrhage.* (Brit. Med. J., April 2, 1949, 572-574).

All 3 cases of intra-abdominal bleeding presented had evidence of hypertension. In the first case there was no morbid anatomical source of the hemorrhage apart from hypertensive changes in the smaller vessels. The second case showed intramuscular hematomata, and hypertensive arteriolar disease accounted for the accident. The third case showed a hemoperitoneum from rupture of a perirenal hematoma, and there was clinical evidence of hypertension.

MACKEERAS, M. J. AND MACKEERAS, I. M.: *The prevention of gastro-enteritis in infants.* (Med. J. Australia, April 9, 1949, Vol. 36, No. 15, 477-482).

The authors have studied the title problem from the bacteriologic and hygienic standpoints and believe that the most

important elements in the prevention of infantile gastroenteritis are strict separation of the duties and scrubbing-up facilities of "clean" and "change-up" nurses; institution of "infectious disease" techniques for all nurses, doctors and students; careful disposal of soiled napkins; preparation of the feedings of infants in a separate properly designed and equipped "formula room" and sterilization of the feedings in complete covered units before they are sent to the ward.

OGLIVIE, SIR HENEGAGE: *In praise of idleness.* (Brit. Med. J., April 16, 1949, 645-651).

In a speech packed with much sane philosophy, Ogilvie comes down to cases and grapples with the "stress" diseases, thyrotoxicosis, duodenal ulcer and hyperpiesis (non-renal hypertension). He believes that thiouracil has had a fair trial and has failed miserably and ought not to be used except in case where resection has been abandoned or where it must be postponed until after the performance of another and more urgent operation, such as one for cancer. He notes the increase in duodenal ulcer in women. He reserves vagotomy for patients who experience a return of pain or ulceration after radical gastrectomy, for marginal ulcer, and for old men whose duodenal pain is out of proportion to the very moderate ulcer that seems to be causing it. Radical gastrectomy, Billroth I or the valvular Billroth II, are the author's choice in treatment. He cannot recommend the Smithwick operation for hypertension and calls it a "Peet-Adson hybrid." He accepts only cases for operation which have received no benefit from intelligent medical treatment and he refuses no cases, except those with advanced myocardial damage. He does a bilateral subdiaphragmatic operation, resecting the 12th rib, removing the sympathetic chain from the 3rd lumbar to the 12th dorsal ganglion. He divides the splanchnics where they enter the semilunar ganglion and follows them as high as possible through the diaphragm before cutting them again. This operation is unilateral or bilateral, depending on the patient's condition. After 3 months' rest, if necessary, he removes the 2nd, 3rd and 4th thoracic ganglia, first on the left side and later, if necessary, on the right side. An operation that, judged by the sphygmomanometer, is a failure, may in many cases relieve the patient of all his distressing symptoms. In all stress diseases, prevention is better than cure and what man needs today is work that is interesting. He also needs hope and opportunity and novelty. He says the world no longer is full of opportunity. The article suggests a broad frustration as a basis for stress.

GABERMAN, P.: *Extrarenal azotemia and lower nephron syndrome.* (Ill. Med. J., May 1949, Vol. 95, No. 5, 292-298).

The "lower nephron syndrome" is a term replacing such older names as acute Bright's Disease, acute parenchymatous nephritis, and acute tubular nephritis. The syndrome affects essentially the cells of the kidney tubules, particularly those of the ascending loop of Henle and the distal convoluted tubules. The common causal factor probably is anoxia. So-called extrarenal azotemia probably is the same syndrome. The most commonly met mechanisms, alone or in combination, are shock, hemorrhage, hemoglobinuria, liver damage, physicochemical alterations in the blood leading to acidosis, alkalosis and dehydration, increase in protein catabolism and local renal disturbance. The mortality rate is high, about 90 percent. When the disease follows the "crush syndrome" the crushed limb should be at once bandaged to prevent absorption of toxic products. Peritoneal lavage may prove helpful. Prophylaxis is of major importance.

BRODY, E. B.: *Psychologic tension and serum iodine levels in psychiatric patients without evidence of thyroid disease.* (Psychosom. Med. Mar.-Apr. 1949, Vol. XI, No. 2, 70-73).

The author examined the serum iodine levels of 125 patients from the Psychiatric Clinic of Yale University School of Medicine and found that those with the highest levels could be classified as showing a higher level of psychological tension while those with lower iodine levels manifested a lower degree of psychic tension. None of the patients so examined

showed thyroid disease. These findings may reflect gradual increases in thyroid activity (within the 'normal' range) associated with repeated psychologically stressful experiences. Increased thyroid secretion may result from the stimulation of anterior pituitary thyrotrophic hormone output by adrenergic substances discharged during stressful experience.

HIGHTOWER, N. C., JR., CODE, C. F., AND MAHEU, F. T.: *A method for the study of gastro-intestinal motor activity in human beings*. (Proc. Staff Meet. Mayo Clin., 24, 18, 453-462).

The authors describe a flexible and durable apparatus for recording gastrointestinal motor activity, which has given repeatable recordings from the antrum of the stomach, and the small and the large bowel. Recordings from the antrum show small waves with a 20-second rhythm and also larger hunger-type waves. In the duodenum, more rapid waves of activity are found, along with a base-line deflection which is usually interpreted as due to changes in the tone of the bowel. Equally satisfactory records have been obtained from the small and large bowel. In the latter case estimations have been made via a colonic stoma. The method consists of the use of a balloon (or balloons) attached to a gastric tube which is swallowed. Variations in water-pressure within the balloon are communicated to an air-cushion system which causes a glass spoon manometer to lengthen or contract. A small mirror placed on one end of the spoon reflects a beam of light 1 meter to the aperture of a camera which makes a record on moving film. The authors are cautious in their interpretations but indicate that the method overcomes some of the disadvantages of other balloon systems.

FICARRA, B. J.: *Postoperative fetor oris*. Rev. Gastroent., 17, 12, Dec. 1950, 1151-2.

Bad breath occurring postoperatively may be caused by conditions prior to surgery, such as pyorrhea, dental caries, atrophic rhinitis, bronchiectasis or Vincent's angina. However, the appearance of halitosis may herald the beginning of some complication such as intestinal obstruction, peritonitis, acute gastric dilatation, lung abscess, postoperative parotitis or subphrenic abscess piercing the diaphragm.

KISSINGER, C. C.: *Construction of a permanent skin-covered ileostomy*. J. Indiana State Med. Assn., 44, 1, Jan. 1951.

Kissinger, working at the Fort Wayne Veterans Hospital, performed an ileostomy in which the skin-covered portion of exteriorized ileum resembles a penis and the fecal discharge is easily caught by an ordinary colostomy bag. The patient, who suffers from chronic ulcerative colitis, has greatly improved and returned to work. Soon the author intends to remove the colon, rectum and anus.

WELBORN, M. B.: *Volvulus of the cecum*. J. Indiana State Med. Assn., 44, 1, Jan. 1951.

Welborn describes 2 cases of volvulus of the cecum in elderly women in which detorsion by operation permitted recovery. The author suggests that a band fixing the ascending colon is a necessary prerequisite, furnishing a pivot upon which the mobile cecum may revolve. Sometimes cutting this band is all that is necessary to cure the condition. In other cases, the cecum after detorsion should be anchored to the parietal peritoneum.

MADISON, M. S. AND BARGEN, J. A.: *Fulminating chronic ulcerative colitis with unusual segmental dilatation of the colon*. Proc. Staff Meet. Mayo Clin., 26, 1, Jan. 3, 1951.

The authors report a severe case of chronic thrombo-ulcerative colitis who improved on the medical measures used but who showed a transient, tremendous dilatation of the transverse colon over a period of weeks. There was no obstruction and congenital megacolon was ruled out by the ability of the dilated segment to empty itself. No explanation for this unusual finding was offered.

MOST, H., AND VAN ASSENDELFT, F.: *Laboratory and Clinical Observations on the Effect of Terramycin in the Treatment of Amebiasis*. Ann. New York Acad. Sc. 53: 427 (Sept. 15) 1950.

In this study terramycin in vitro was found to be highly active against cultures of *E. histolytica* with complete inhibition in 24 hours. Marked sensitivity of associated bacteria,

namely *Cl. welchii*, *Streptococcus faecalis* and *E. coli* were also noted in the same cultures.

22 patients with colonic amebiasis diagnosed by the demonstration of *E. histolytica* in the stools were treated with terramycin. 13 patients over 75 pounds were given 2 grams daily in divided doses for 10 days, 9 children under 75 pounds were given one gram daily. Stool examination showed evidence of degeneration of the organism within 48 hours, disappearance of the organism on the third day and found negative up to 93 days. No adverse signs except mushy or loose stools were noted. In addition, the patients harbored other protozoa and parasites on stool examination; of these, *Endolimax nana* and *coli* and *Iodamoeba butschlii* were negative after treatment. However, the helminths and intestinal flagellates were unaffected.

They concluded that it appeared that terramycin will prove to be an extremely valuable agent in the therapy of intestinal amebiasis.

DOWLING, H. F., LEPPER, M. H., CALDWELL, E. R., AND SPIES, H. W.: *Terramycin in the Treatment of Pneumococci and other Bacterial Infections*. Ann. New York Acad. Sc. 53:433 (Sept. 15) 1950.

Sensitivity studies of terramycin, aureomycin and chloromycetin on 27 strains of pneumococci were performed. The activity of terramycin and aureomycin was about the same; however, greater concentration of chloromycetin was needed.

In their clinical studies adult patients were given 2 grams initial dose followed by 0.5 grams at 4 hour intervals until 2-3 days beyond subsidence of active infection; children were given an initial dose of 25 mg per kilo of body weight followed by 42 mg per kilo per kg per day in 6 divided doses. 6 children ages 4-6 years with severe dysentery due to *S. paratypherae*, were treated. In all cases diarrhea stopped within 48-72 hours and the organism disappeared from the stool after treatment was started, and did not reappear. Among other infections studied 48 patients with clinically characteristic pneumococcal pneumonia were treated with good results; 11 patients with streptococcal infections including Scarlet Fever, Pharyngitis and Pneumonia showed rapid improvement; 7 patients with acute urethritis were rendered symptom free with negative smears within 12-48 hours, and with no relapses; 7 to 11 patients with urinary infections recovered completely.

They concluded that terramycin is a potent antibiotic and the results are similar to those obtained when aureomycin is used.

WILLIAM H. DEARING AND GERALD M. NEEDHAM: *The Effect of Terramycin on the Intestinal Bacterial Flora of Patients Being Prepared for Intestinal Surgery*, Staff Meetings of the Mayo Clinic, Volume 26, Number 3, January 31, 1951.

The investigators studied 68 patients with various types of intestinal lesions requiring surgical treatment. Prior to surgery each patient received 750 mg of terramycin orally 4 times daily as well as a diet of minimal residue, a daily saline cathartic and series of enemas before operation. In 44 patients receiving the antibiotic for periods of 1½-4 days all the culturable micro-organisms except *Proteus* and *Pseudomonas*, yeast and certain coagulase-negative micrococci were removed. In 8 patients given terramycin for 3-3½ days it was noted that *Streptococcus faecalis* and *Aerobacter aerogenes* persisted. In 16 patients treated for less than the recommended 3 days, organisms such as *Aerobacter aerogenes*, and *E. coli*, *Streptococcus faecalis* were found. Bacteroides organisms disappeared readily in contrast to the stools of untreated patients. Clostridium organisms were among the first to be eliminated from the stools. Nausea and vomiting were the only untoward symptoms noted and could be reduced to a minimum after the terramycin was given with food. They concluded that terramycin is as effective as aureomycin as an antibacterial agent on intestinal flora.

SIELAFF, HANS-JUERGEN: *Röntgenological finding in metastases of a melanoma in the duodenum and the small intestine*. Fortschr. Röntgenstrahlen 71, 4, 592, August 1949.

The author describes the roentgenological findings of metastases of a melanoma of the back in the duodenum and the small intestine. The patient was 19 years old. Large nodular masses were demonstrated in the duodenum and jejunum. They were round and showed a pathological surface.

There was an invagination present. The excision of the primary tumor may have provoked the spread of the condition.
Franz J. Lust

BUECKEL, J.: *Roentgenological signs of hyperplastic gastritis*. Fortschr. Roentgenstrahlen 71, 2, 1949.

This is an excellent contribution to the roentgenological studies of hyperplastic gastritis. Nodular hyperplasia of the mucosa around a peptic ulcer are demonstrated in the x-ray film and the pathological specimen. A case of antral gastritis is reported in which the roentgen findings were irregularity of the antrum, slight pyloric stenosis, simulating a malignancy. Besides, the état mamelonné is shown and changes producing multiple, small polyps of the mucosa.

Franz J. Lust

PLUMMER, GEORGE W. AND STEBINS, SAMUEL J.: *Bleeding duodenal ulcer in infancy: A surgical problem*. J. Pediatrics 37, 6, 899, Dec. 1950.

Two cases in female infants under one year of age are reported successfully treated by surgery during acute hemorrhage. Bleeding duodenal ulcers should always be seriously considered in the differential diagnosis of gastrointestinal hemorrhage in infancy. Hematemesis is not necessarily the criterion to establish the diagnosis.

The margin of safety in conservative treatment of this condition of the infant is considerably reduced in contrast to that of the adult. The advances in preoperative and postoperative care combined with modern surgical technique remove this condition from the hopeless field of therapy.

Franz J. Lust

CARTER R. F. AND GILLETTE, L., NEW YORK: *Benign stricture of the intrahepatic bile ducts*. J. A. M. A., 145-6 pp. 375-379, Feb. 1951.

The authors report on 15 cases where a benign stricture of the intrahepatic bile ducts was observed. The site of the stricture was within the liver substance at the level of the union of the two hepatic ducts.

An ulcerative cholangitis seemed to be the etiology although no histologic studies have been carried out. However the regular location within 3 cm. of the union of hepatic ducts would suggest a primary congenital anomaly.

In 10 out of 15 cases the bile above the stricture was infected and positive cultures were obtained, with B. coli in the majority.

The clinical picture was that of an obstructive jaundice with chills, fever and progressive jaundice.

As treatment, dilatation of the place of the stricture with placement of the T-tube was successful; in others an anastomosis of the dilated hepatic duct with the duodenum was done. The T-tube was left in some cases over a year.

Hepatico duodenostomy was done in 10 cases, in two a hepatico-cholecystostomy was performed. Results were good in 11 cases in a follow up from 1 month to 2 years and 9 months.

B. O. C. Pribram, New York

BERNING, HEINRICH: *Clinical and roentgenological examinations of the dilatation of the stomach*. (Klinisch-roentgenologische Untersuchungen ueber die Magendilatation). Fortschr. Roentgen 73, 2, 165, June 1950.

The object of this paper was the functional gastric tonus and the dilatation of the stomach without anatomical obstacle, characterized by metabolic disturbance with keto anemia. Especially the dilatation of the stomach in diabetogenic coma, in acetone vomiting of children and the loss of tonus following operation were studied clinically and roentgenologically. Acute dilatation and loss of gastric tonus is observed in absolute heterogenous diseases, but disturbance of metabolism seems the same in all instances. Multiplication of ketobodies in the blood and its paralyzing effect are playing a dominant role. In treating the disturbance of metabolism best results may be achieved in cases of stomach dilatation without anatomical obstacle.

Franz J. Lust

INGRAM, JR., M. D.: *Gastric ulcer in childhood*. A. J. Roentgen. & Rad. Th. 64, 5, 765, Nov. 1950.

Gastric ulcer in children is a rare occurrence. Of the thirty-three cases reported in the literature, five were found

at autopsy, thirteen by surgery, and fourteen by roentgen study. Nine of the latter group were confirmed by surgery. It is interesting to note that the first four cases reported in the literature were found at autopsy, the next thirteen cases were found at surgery. Of the remaining cases reported since 1932 (15 cases) all but three were initially diagnosed from the roentgen examination. The table gives ample evidence of the increasing frequency with which the diagnosis of gastric ulcer in childhood has been made with the use of the roentgen examination. It points out the importance of subjecting all children with gastrointestinal symptoms, especially hemorrhage, to a thorough roentgen study of the gastro-intestinal tract. The author reports the case of an eleven year old child with a gastric ulcer, which was treated medically.

Franz J. Lust

RAVITCH, MARK M. AND McCUNE, ROBERT: *Intussusception in infants and children*. J. Pediatrics 37, 2, 153, Aug. 1950.

Intussusception is a condition which should be free from mortality if treated in the first 24 hours after onset of symptoms. Preoperative administration of parenteral fluids and blood is of sufficient importance to warrant priority over definite therapy, especially in the late cases. Hydrostatic pressure reduction under fluoroscopy appears to give both a lower mortality and a lower morbidity than primary operative reduction as measured by fever, diarrhea, vomiting, distention, length of hospital stay, wound infections, and mechanical intestinal obstruction due to adhesions. If resection is required, anastomosis with an associated vent seems the safest method.

Franz J. Lust

BOEHM, F.: *The roentgenological appearance of the healed, formerly ulcerated tuberculosis of the intestine*. (Die roentgenologischen Erscheinungsformen der abgeheilten, ehemals geschwuerigen Darmtuberkulose) Fortschr. Roentgenstrahlen 72, 6, 675, April 1950.

Healing of intestinal tuberculosis leads to characteristic roentgen signs, the explanation of which is based on anatomical findings. These are: fine superficial star-shaped deformations of the mucosal pattern, larger patches with atypical slightly polypoid intramural surface, thickening and stiffness of the bowel wall, longitudinal shrinking especially of the colon and intestinal obstruction. Accordingly, the normal mucosal pattern shows roughening and deformities, larger areas of coarsely, granular intramural surface, localized rigidity and ruggedness of the bowel wall. The colon seems shortened, the passage slow. A pouch-formed cecum seems characteristic. The knowledge of these roentgen signs may turn out important, as intestinal tuberculosis sometimes heals without any clinical significance. The illustrations of this article are excellent.

Franz J. Lust

VOGT, ALFRED: *Esophagitis*. Fortschr. Roentgenstrahlen 72, 6, 686, April 1950.

Three observations of esophagitis are reported. The first one was found in a case of lymphosarcomatosis. In the second case, a lymphogenous leukemia was present. The mucosal folds were hypertrophic and the mucosa had an interwoven structure. In the last case a peptic ulcer of the esophagus was present. The folds were broad, swollen, stiff, and had a longitudinal pattern.

Franz J. Lust

HORNKIEWYTSCZ, TH.: *Contributions for the differential diagnostic of niches of the greater curvature of the stomach*. Fortschr. Roentgenstrahlen 71, 6, 906, Oct. 1949.

Three cases with niches of the greater curvature of the stomach are reported. In the first patient, a benign ulcer, like a diverticulum was found. In the second case a large niche was demonstrated without involvement of the folds of the stomach. This turned out to be a carcinoma. In the third case a scirrhus of the stomach was present, the center of which had undergone extensive ulceration. The author stresses the difficulties in differentiating these malignant conditions from ulcers.

Franz J. Lust

AMER. JOUR. DIG. DIS.

NEW JELLY FORM FOR NASAL ITEM

To facilitate intranasal administration of Neo-Synephrine and Thenfadil, the decongestant and antihistaminic preparation, Winthrop-Stearns Inc. will introduce it in a light water-soluble jelly form on May 14. The preparation comes in a 5/8 ounce collapsible tube from which the patient squeezes a small amount and sniffs it back to cover the intranasal area. It is supplied one tube to a carton, and twelve tubes are packed in a shelf carton.

The preparation contains Neo-Synephrine hydrochloride 0.5 per cent and Thenfadil hydrochloride 0.1 per cent. Basis of the use of the two in combination is the fact that antihistaminic compounds such as Thenfadil, along with a decongestant, benefit nasal allergy when applied nasally, according to clinical experience cited in company literature. Neo-Synephrine hydrochloride is reported to have a low toxicity, prolonged decongestive action, and lack of central stimulating or depressing effect.

In combination with Thenfadil, potent antihistaminic, it is indicated for the temporary relief of congestion in allergic rhinitis, including hay fever, vasomotor rhinitis and sinusitis.

COURSE IN POSTGRADUATE GASTROENTEROLOGY

The National Gastroenterological Association announces that its course in Postgraduate Gastroenterology will be given at the Drake in Chicago, Illinois on September 20, 21, 22, 1951.

This year the course will again be under the direction and co-chairmanship of Dr. Owen H. Wangenstein, Professor of Surgery of the University of Minnesota Medical School, who will serve as surgical co-ordinator and Dr. I. Snapper, Director of Medical Education of The Mount Sinai Hospital, N. Y., N. Y., who will serve as medical co-ordinator.

Drs. Wangenstein and Snapper will be assisted by a distinguished faculty elected from the medical schools in and around Chicago whose presentations will cover the following subjects: diseases of the mouth, diseases of the esophagus, peptic ulcer, diseases of the stomach, diseases of the pancreas, cholecystic dis-

ease, psychosomatic aspects of gastrointestinal disease, diseases of the liver, diseases of the colon and rectum, and other miscellaneous subjects including pathology and physiology, radiology, gastroscopy, etc.

For further information and enrollment write to the National Gastroenterological Association, Department GSJ, 1819 Broadway, New York 23, New York.

LILLY'S TO PROCESS BLOOD PLASMA

Because stock-piling of human blood plasma for military or civilian disaster is considered an essential defense measure, Eli Lilly and Company has announced plans to establish a modern blood-processing unit. Over 2,000,000 pints of blood were processed and supplied at cost by the Lilly company during World War II. The unit, to be set up and operated in Indianapolis for the Armed Services Medical Procurement Agency of the United States, will be completed late this year.

Whole blood collected in principal Midwestern cities by the Red Cross will be expressed to the Lilly plant in refrigerated containers. Almost immediately after the whole blood arrives, processing starts with the centrifugation of plasma from the cells. The plasma is drawn off, pooled, and irradiated with ultraviolet light. The latter step has been added since World War II and is designed to inactivate one virus responsible for hepatitis. The plasma is then shell-frozen against the inside surface of a rotating bottle. Drying is accomplished by controlled temperature and high vacuum. Rigid aseptic techniques are followed in processing, and all plasma must pass sterility tests. Plasma will be packaged in a sealed moisture-proof container with a companion bottle of sterile diluent. Sterile tubing and hypodermic needles will complete the unit, which will provide ready-to-administer plasma at the scene of injury.

Professional Relations Dept.

OPPOSES FEDERAL SUBSIDY FOR MEDICAL EDUCATION

Current proposals before the U. S. Senate for direct federal subsidies to aid the country's medical schools would "introduce a new pattern" for government financial support to colleges and universities and would

endanger "the intellectual heritage of freedom and diversity which characterizes American higher education."

This conclusion is reached by the Commission on Financing Higher Education in its statement, "Financing Medical Education." The statement is the second analysis of special needs in financing higher education, developed as a part of the Commission's long range study of the whole problem. Composed of 12 business and educational leaders, the Commission is financed by the Rockefeller Foundation and the Carnegie Corporation and is sponsored by the Association of American Universities.

Senate Bill No. 337, now awaiting floor action, would authorize grants to all accredited medical schools on a per student basis, the statement notes. "Such a change needs much more thought than it has yet had," the Commission points out. "Our views are definite; we do not wish to see an expansion of direct federal financial subsidization of higher education in this country. If medical education should be directly subsidized, other educational programs might also claim such support."

"Until it has been clearly demonstrated that other sources of support cannot finance medical education, we believe no such great and potentially far-reaching innovation in federal financing should be undertaken," the Commission emphasizes.

MEDICAL SCHOOLS NEED MORE SUPPORT

At the same time, the statement stresses that the rising cost of medical education and the nation's demand for more doctors and greater medical facilities make imperative the need to provide more income for medical schools.

"If other sources of income fail to provide the kind of medical education this country demands, the American public may insist upon federal government support," the Commission warns. "The medical education of today, the medical service of tomorrow, the financial future of many important universities depend upon how this country meets the challenge of more medical school income now."

Analyzing the present support given to medical education, the statement reports that it took \$70,000,000 to operate the 72 four-year medical schools in the U. S. in

1950—less than 50 cents per person for our population of 150,000,000. A minimum of another \$40,000,000 a year is needed to cover the medical schools' operating expenses at present enrollment levels according to the Surgeon General's office, the Commission notes. Even more money is required to expand the physical facilities needed to teach medicine.

For colleges and universities with medical schools, however, the task of providing for their support constitutes "the most pressing single financial problem" of these institutions, the statement says. A sampling of 18 private and 18 public universities reveals that at least 20% to 30% of their teaching budgets go to their medical schools, although the medical students form only a small percentage of the total students, in some cases, as little as 2%. Universities with little endowment must divert income from fees paid by all students, the survey shows, to support the medical schools, with serious consequences for the non-medical fields.

Either additional money must be found or universities will have to divorce themselves from medical schools to preserve their other functions, the Commission concludes. It is opposed to such a separation, however, since university affiliation helps to make medical education "a science dedicated to constant enlargement of human knowledge." Most great advances in medicine have come from university medical schools, the statement points out.

NEW SOURCES OF INCOME

The Commission suggests the following alternatives to federal subsidy:

1) More economies in medical schools are needed to eliminate costly practices. Medical schools "have not yet demonstrated to outside satisfaction that their operations are economical and efficient," the Commission notes, warning that outside investigation may be necessary if medical educators cannot achieve such economies.

2) Hospital care and other community services now provided by medical schools should be financed by patient charges or by local government appropriations for welfare purposes. Noting that the finest medical care in the U. S. is provided by medical schools and their

teaching hospitals, the Commission maintains that "the individual and the community should be prepared to meet the costs of such service."

3) Foundations, corporations and other agencies supporting medical research should bear the full costs of such research. The indirect costs of research should not, as they now do, burden the hard-pressed medical school budget. A minimum of 25% should be allowed for indirect costs on any research rather than the inadequate 8% now customary.

4) States should increase their appropriations for medical education through new tax revenues, but not at the expense of other state-supported programs of higher education.

5) Gift income for medical schools should be increased. If every physician contributed on an average \$100 a year to medical education, nearly \$18,000,000 in new income would be provided, the Commission suggests. It also recommends more corporate support of medical education as well as research and notes that the newly organized National Fund For Medical Education offers appropriate machinery for such contributions.

OPPOSES INCREASED STUDENT FEES

No substantial new income for medical schools should be sought through a general increase in tuition fees, according to the Commission. Such fees are already higher than for any other university course of study and, as a profession, medicine demands the longest period of preparation and the greatest overall cost. The statement stresses that "there is social danger in erecting economic barriers to medical education."

Contributing to the necessarily high cost of medical education are: the individualized, graduate-level type of training; high faculty salaries to attract competent full-time staff members, against high-income competition of private practice and the expensive but essential medical research to keep medical education alive and productive.

Medicine's achievements in growing control of disease, increasing longevity and improved quality of medical care is largely "the direct consequence of our system of medical education, with its double emphasis upon instruction and research." But these advances have been purchased at a price,

the Commission warns: "The costs of medical training have now been pushed so high as to make its financing a major national problem."

AMERICAN CAN CO. CITED FOR PUBLIC SERVICE RECORD

The American Can Company at its 50th anniversary dinner recently was cited by the National Canners Association for distinguished service to the progress of the canning industry and to a higher standard of living for the American public.

Presentation of the citation by Carlos Campbell, executive secretary of NCA, to C. H. Black, president of the container manufacturing firm, was heard by almost 1,400 employees attending the dinner at the Waldorf-Astoria Hotel. It also was heard over one of the most extensive long distance telephone hook-ups in industrial history by the company's 34,000 employees at 70 other simultaneous birthday dinners in the United States, Canada and Hawaii.

The NCA citation commended Canco for its contributions to the presented to all employees who have container making and canning industries through its own engineering and research laboratories, its support of NCA's research work and its assistance to individual canners.

"These magnificent efforts," the citation said, "have not only resulted in the development of better processing techniques and better precision-built containers for both old and new products. They have also contributed largely to the advancement of the canning industry and to making available to the public in peacetime—and to the armed services in national emergencies—an abundant supply of diversified canned foods at reasonable prices."

"These have been great achievements, possible only to an organization endowed with unique managerial efficiency, blessed with high-calibre employees, and dedicated to the highest principles of American business enterprise," Mr. Campbell said in making the presentation.

Accepting the NCA citation on behalf of the company, Mr. Black called on every member of the firm's organization "to join with me in the firm resolve that, come what may, war or peace, each of us will continue to do everything in his

power to maintain the standards of service to the customer and the public that have been established at Canco during these 50 years."

"As we enter a new half century, I know that the spirit of Canco that has sustained us in the past will help us to expand and constantly improve the service we render to all those who depend upon us for the best products and service that we can provide," he said.

D. W. Figgis, chairman of the board of directors, inaugurated the company's new long service emblem program by presenting a gold lapel insignia to George Wilhelm, Canco's New York area employee with the longest service record. Mr. Wilhelm, who has been with the company since the time of its organization, is associated with the Metropolitan district sales organization.

Other service emblems are being presented to all employees who have been with the company for five or more years. The company reports that 47 per cent of its 34,000 employees are eligible to receive the long service insignia.

Presenting the long service emblem to Mr. Wilhelm, Mr. Figgis stressed the importance of good human relations to Canco's progress during its first half century. "We've arrived at this milestone of success by working together as stockholders, as managers, as individual members of a constantly growing and constantly changing team, banded together for the mutual advantages of profit, security and achievement," he said.

W. C. Stolk, executive vice president, made a symbolic presentation of the company's 50th anniversary flag to R. L. Sullivan, vice president in charge of the Atlantic Division. Mr. Sullivan accepted the flag on behalf of employees of the firm's four divisions.

Messages were heard over the long distance telephone hook-up from Chicago by M. P. Cortilet, vice president in charge of the Central Division; from San Francisco by C. W. Roberts, vice president in charge of the Pacific Division; and from Hamilton, Ontario, by Gordon Mann, general manager of the Canadian Division.

Mr. Stolk served as master of ceremonies for the dinner program.

Other anniversary dinners were held in the New York area last night for employees of the company's

plants in Brooklyn, Jersey City, Hoboken, Newark and Hillside, N. J.

NEW PHARMACEUTICALS DEVELOPED IN INSTITUTE IN YEAR

Rensselaer, N. Y.—Important new introductions for pharmaceutical and industrial applications developed at the Sterling-Winthrop Research Institute were disclosed today (Thursday) by James Hill, Jr., chairman and president of Sterling Drug Inc., in a review of the Institute's first year of operation. The Institute, which conducts basic scientific research for the various units of the Sterling organization, was dedicated on May 17, 1950.

"The first year has been largely an orientation period, in which our new laboratory equipment and procedures were constantly being developed and installed preliminary to full attack on the research program," Mr. Hill said. "Even during this shakedown period, Institute scientists successfully synthesized and laboratory-tested a large variety of preparations—some of which have gone into commercial manufacture."

Winthrop-Stearns Inc. introduced among other products a new hormone called Levophed, for acute hypotensive states such as post-operative shock, and will shortly supply physicians with a newly developed, synthetic curare-like drug used as a muscle-relaxing agent during surgery; and a new combination of Aralen and Milibis, potent antimalarial and amebicide, to help control the world's two most infectious diseases.

George A. Breon & Co., which details physicians, made available Transibarb capsules indicated in the menopause syndrome of the elderly, which also minimizes nervous apprehension in debilitated and mentally depressed patients; and Duco-bee brand of Vitamin B12 for pernicious and secondary anemia, especially for patients hypersensitive to liver and liver extracts.

Cooke-Waite Laboratories Inc., producers of preparations used by dentists, introduced Dynium chloride, a new quaternary ammonium antiseptic employed as a cold sterilizing solution. Sterwin Chemicals Inc., suppliers of bulk vitamin products, introduced a number of enrichment mixtures for human foods

as well as for livestock and poultry feeds.

The veterinary division of Winthrop-Stearns made available to small animal practitioners Pentobrocane, an injectable barbiturate for anesthesia; Testocaptate, a synthetic male sex hormone of increased potency; and an injectable form of Aralen for treatment of anaplasmosis, a malaria-like disease afflicting cattle.

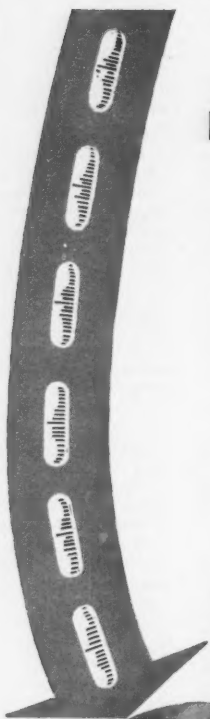
Research on such preparations is conducted by a staff of scientists, who come from more than 100 colleges and universities, and from 12 different countries, Dr. Maurice L. Tainter, director of the Institute said. Last year, he explained, they prepared approximately 75 scientific papers, read at meetings and published in technical journals. In addition, a series of weekly seminars and symposia is conducted for the staff members.

CITIZENS COMMITTEE FOR THE HOOVER REPORT

New York.—Dr. Robert Collier Page, Chairman of the National Doctors Committee for Improved Federal Medical Services, has announced the completion of an advisory committee of experts from every branch of the medical profession. They will consult with the Chairman on matters of policy in the pending campaign to secure wide economies and more efficiency in the present overlapping and competing system of hospital and medical care operated by the government. Dr. Page, who is Medical Director of Standard Oil Company (New Jersey), also announced that his general committee will carry on an educational program for the benefit of 178,000 doctors. He said that this project is rapidly growing.

The National Doctors Committee is an affiliate of the Citizens Committee for the Hoover Report, which is urging passage of the recommendations of the bipartisan Hoover Commission for the unification of the various governmental medical agencies under a single authority. The slogan of the Doctors Committee is "Not more government in medicine but better medicine in government."

"The interest in our general committee is surprisingly large, and very widespread," Dr. Page



DIAGNOSIS CAN BE DEFINITE!

because...

- ① **MONOPHEN** "normals" are consistently sharp and clear.
- ② Diseased gallbladders visualize poorly or not at all.
- ③ This diagnostic trustworthiness has been attested to by its use in over 3000 cases... *with complete confirmation of those cases where surgical intervention was recommended.*

In addition, the proven infrequency of side reactions such as cramps, diarrhea, dysuria and nausea, makes the easily swallowed **MONOPHEN** capsules ideally suited for routine use, particularly since double doses are unnecessary.

Wasch, Milton G. and Epstein, Bernard S.: Am. J. Roentgenol. & Rad. Ther., 66:98-102, 1951. **MONOPHEN**—A New Medium for Cholecystography.

Epstein, B. S., Natelson, S. and Kramer, B.: Am. J. Roentgenol. & Rad. Ther., 58:301-307, 1946.

MONOPHEN

THE MODERN CHOLECYSTOPAQUE

BELL-CRAIG, INC.
formerly
NATIONAL SYNTHETICS, INC.
270 Lafayette Street, New York 12

"Dependability Through the Years"

WHY DON'T YOU TRY MONOPHEN?

MONOPHEN is 2-(4-hydroxy-3, 5-diiodobenzyl)-cyclohexane carboxylic acid, containing 52.2% iodine in stable combination.

SUPPLIED IN BULK: Capsules (0.5 gram) are cellophane-sealed and boxed in quantities of 50, 100, 250, 500 and 1000 with a requisite number of dispensing envelopes imprinted with directions for use.

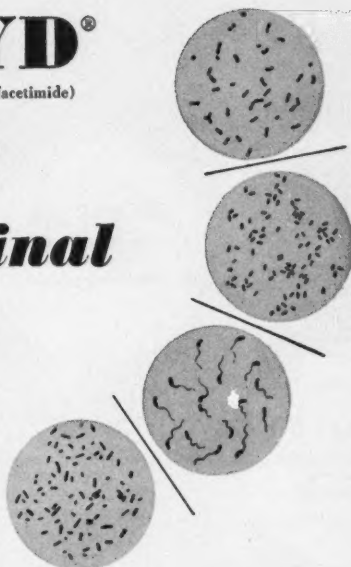
Write for samples

THALAMYD®

(brand of phthalylsulfacetimide)

eliminate
intestinal
organisms

SIMPLY
AND
SAFELY

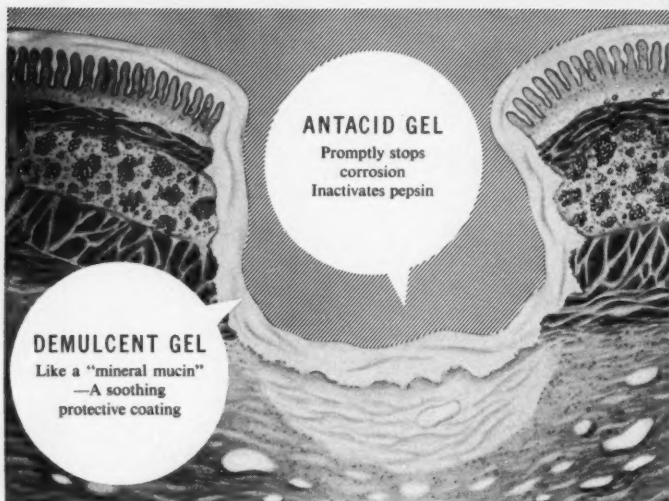


Unique among nonabsorbable sulfonamides, THALAMYD is actually absorbed into the bowel wall in high concentration but only slightly absorbed into the blood stream.

Simple, safe therapy whenever the intestinal tract must be sterilized, THALAMYD has a broad field of usefulness: *prophylactically when preparing the gut for surgery; for bacillary dysentery and other acute enteritis; and to control secondary invaders in ulcerative colitis.*

Schering CORPORATION • BLOOMFIELD, NEW JERSEY





In the Medical Management of Peptic Ulcer

AMPHOJEL Has Double-Gel Action

Relieves pain in minutes

Promotes rapid healing of ulcers

AMPHOJEL is Safe—does not interfere with normal body metabolism. No danger of alkalosis or acid rebound.



AMPHOJEL is pleasant to take, and is inexpensive.

SUPPLIED: Bottles of 12 fl. oz.

AMPHOJEL[®]

ALUMINUM HYDROXIDE GEL
ALUMINA GEL WYETH

Wyeth Incorporated, Philadelphia 2, Pa.

Lubricoid action

WITHOUT OIL IN CONSTIPATION

Turicum combines methylcellulose in hydrated form with magnesium hydroxide in less-than-laxative dosage to maintain hydration throughout the bowel.

The methylcellulose passes through the stomach and small intestine without digestive breakdown; mixes with the fecal residue in the colon, incorporating dry particles in its mass.

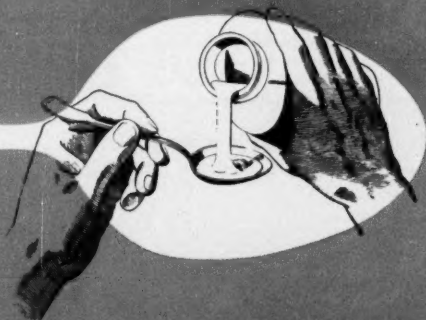
The osmotic effect of magnesium hydroxide assures the presence of adequate water as the dry fecal material is brought into the gel. Thus easy passage is accomplished without stimulant cathartics.

Turicum is unique as a non-oily lubricoid, fecal-softening agent, acting in a rational manner to restore the normal pattern of bowel function. With Turicum there is no bloating—no danger of impaction, lipid pneumonia or leakage, and no interference with utilization of oil-soluble vitamins.

Average dose: one to two tablespoonfuls.

Available in pint bottles.

TURICUM®
HYDROPHILIC LUBRICOID



Whittier
LABORATORIES

DIVISION NUTRITION RESEARCH LABORATORIES, INC.
CHICAGO 11, ILLINOIS

Meat... and the Role of Protein in Resistance to Infectious Disease

According to accumulated evidence, an adequate intake of high biologic-quality protein is needed for the generation¹ and active phagocytic functioning of leukocytes^{2,3} and lymphocytes as well as for the fabrication of effective amounts of antibody globulin.⁴ Both the natural and the acquired capacities of the body to counteract the pathologic stimuli of infectious disease, in considerable measure, hinge on adequate protein nutrition.⁵

Substantiating the foregoing clinical conviction, recent studies have demonstrated that protein-depleted animals subjected to pathologic stimuli display a greatly lowered capacity for manufacturing specific antibodies.⁶ Conversely, repletion of their protein stores with high-quality protein quickly restores a normal capacity for antibody production. Furthermore, protein-depleted animals are both more susceptible to induced infection and less responsive to immunization than those well nourished.

Findings such as these and the fact that human antibody globulin is a highly complex protein containing all the essential amino acids justify the following authoritative deductions⁶:

a. Lacking an adequate supply of essential amino acids, the body manufactures antibody globulin with difficulty, and

b. Because of depleted protein reserves and inadequate intake of essential amino acids, persons long and seriously undernourished manifest increased susceptibility to infection due to inability to fabricate new supplies of antibody globulin.

Because of its rich content of high biologic-quality protein providing all the essential amino acids, meat can play a prominent role in maintaining the body's resistance to infection both in health and disease. Meat can be eaten in adequate quantity daily to assure a significant intake of biologically complete protein.

1. Cannon, P. R.: The Importance of Proteins in Resistance to Infection, *J. A. M. A.* 128:360 (June 2) 1945.

2. Strumia, M. M., and Boerner, F.: Phagocytic Activity of Circulating Cells in the Various Types of Leukemia, *Am. J. Path.* 13:335 (May) 1937.

3. Mills, C. A., and Cottingham, E.: Phagocytic Activity as Affected by Protein Intake in Heat and Cold, *J. Immunol.* 47:503 (Dec.) 1943.

4. Elman, R., and Cannon, P. R.: Protein Malnutrition, in Jolliffe, N.; Tisdall, F. F., and Cannon P. R.: *Clinical Nutrition*, New York, Paul B. Hoeber, Inc., 1950, chap. 7, p. 192.

5. McLester, J. S.: *Nutrition and Diet in Health and Disease*, ed. 5, Philadelphia, W. B. Saunders Company, 1949, p. 347.

6. Cannon, P. R.: Recent Advances in Nutrition with Particular Reference to Protein Metabolism, Lawrence, Kansas, Univ. of Kansas Press, 1950, p. 19.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.



American Meat Institute
Main Office, Chicago...Members Throughout the United States



Are your gallbladder patients tired of a fat-free diet?



OXSORBIL* Capsules are specifically formulated for the large number of such patients. Besides time-proven ingredients to promote the flow of bile and assist in the evacuation of a static gallbladder OXSORBIL Capsules contain a new enormously efficient non-toxic fat emulsifier^{1,2}.

SORBITAN MONOOLEATE POLYOXYETHYLENE DERIVATIVE.

This fat-emulsifier permits the inclusion of larger quantities of suitable (dairy and vegetable) fats—for their highly desirable physiologic chologogic action . . . and also to improve the patient's nutrition.

The administration of OXSORBIL Capsules thus speeds the return to a more normal diet and facilitates the physiological rehabilitation of gallbladder patients.

INDICATIONS: In Chronic Cholecystitis, Non-calculous Cholangitis, Post-cholecystectomy Syndrome, Biliary Dyskinesia, Biliary Stasis without Total Obstruction.

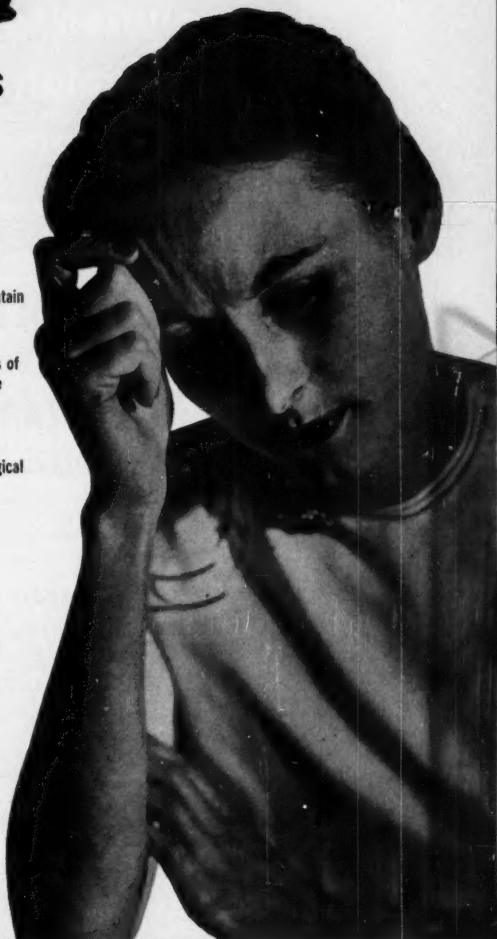
FORMULA: Each Oxsorbil Capsule contains:

Dehydrocholic Acid	½ grain
Desoxycholic Acid	½ grain
Extract of Ox Bile, U.S.P.	1 grain
Sorbitan Monooleate Polyoxyethylene Derivative	2½ grains
Oleic Acid, U.S.P.	2¼ grains

DOSAGE: One to two capsules three times a day or as directed by the physician.

SUPPLY: In bottles of 100 capsules.

REF.: 1) Jones, C. M., et al.: Ann. Int. Med. 29:1-10, July 1948
2) Becker, G. H., et al.: Gastroenterology 14:80-91, Jan. 1950



IVES-CAMERON COMPANY, INC.

22 EAST 40th STREET NEW YORK 16, N. Y.



*Trade Mark

Here is a more
complete
solution to
the weight
reduction
problem...

THE 60-10-70 DIET

THIS PLAN

Plus Obedrin

60-10-70 DIET

NAME _____ DATE _____

WEIGHT _____

DO NOT EAT EVEN SMALL AMOUNTS OF ANY FOOD NOT ON THIS LIST

BREAKFAST

Choose only one item on the list. No Sugar — No Butter.

Scald orange
Orange juice, 1/2 glass (1 oz.)
1 Medium peach
Pineapple (1 slice or
1/2 cup, sliced)
Pears, fresh, 1
Tangerine, 1

Add any one item on the list.

Bread, 1 slice (white, rye, or
whole wheat)
Custard, cracker, 1
Jelly, cream, 18

Choose one average. Serve with vegetables.
Tea or coffee, as usual, no sugar—no cream.
Skimmed milk, 1 glass

LUNCH

Choose one, either meat or fish, not both.

Salmon, 1/2 cup
Loin, 1 slice
Veal, 1 slice
Ham, 1 slice
Beef, 1 slice
Chicken, 1 slice
Ground beef, 1 slice

Choose one average. Serve with vegetables.
Tea or coffee, as usual, no sugar—no cream.
Skimmed milk, 1 glass

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CURBS THE APPETITE

Through the use of the unique 60-10-70 diet and Obedrin tablets, considerable weight can be lost without troublesome hunger or impairment of nitrogen balance. Patient cooperation is assured because morale is kept high and excessive fatigue due to a nutritionally unsound diet is avoided.

MAINTAINS GOOD NUTRITION

The 60-10-70 diet allows free choice of many foods and supplies 70 Gm. of protein, 60 Gm. of carbohydrate, and 10 Gm. of fat, approximately 610 calories. The diet sheets are complete and self-explanatory, making it easy for the patient to do his share.

Obedrin permits adequate dosage of Semoxydrine Hydrochloride (methamphetamine) to suppress appetite. The corrective dose of pentobarbital cancels excessive central nervous stimulation, while vitamins help maintain the patient's sense of well-being.

FORMULA

Semoxydrine
Hydrochloride..... 5 mg.
Pentobarbital Sodium 20 mg.
Ascorbic Acid.....100 mg.
Thiamine
Hydrochloride..... 0.5 mg.
Riboflavin..... 1 mg.
Niacinamide..... 5 mg.

Obedrin is supplied in bottles of 100, 500, and 1,000 yellow grooved tablets.



THE S. E. MASSENGILL COMPANY
Bristol, Tenn.-Va.
NEW YORK • SAN FRANCISCO • KANSAS CITY

SEND FOR YOUR COMPLIMENTARY
COPY OF 60-10-70
DIET SHEETS TODAY

Obedrin

straining at stool:
*always distressing . . .
 frequently dangerous
 . . . sometimes deadly*

The very states in which straining at stool can be most dangerous are conditions which invite constipation: cardiac dysfunction, hernia, pregnancy, anorectal disease and postsurgical states. In their presence, such almost unavoidable factors as inactivity, dietary restriction, weakness and local trauma lead to constipation due to bowel stasis, bulk deficiency or dyschezia.

Prevention of the need to strain has become an important part of therapy in such states. Fortunately, natural, comfortable bowel function can be achieved and maintained with Cellothyl without fear of interference with other therapeutic measures or of inducing cathartic addiction.

Where constipation exists, it can be corrected with Cellothyl; where it is likely to occur, it can be prevented. The ease and frequency of bowel movements improves as Cellothyl reestablishes normal function by correcting several common and related factors:

1. *bulk deficiency . . . by providing adequate bulk of proper consistency*
2. *intestinal stasis . . . by encouraging peristaltic action through gentle mechanical stimulation*
3. *dyschezia . . . by assuring soft, moist, easily passed stools.*

The physician using Cellothyl has the advantage of providing medication which is nontoxic, nonantigenic and nonreactive in the gastrointestinal tract. It causes no bloating or distention, no frequent, urgent calls to stool. Its action is physiologically correct. Following the normal digestive gradient, Cellothyl passes through the stomach and small intestine in a fluid state, then thickens to a smooth gel in the colon, providing bulk where bulk is needed for soft, formed, easily passed stools. The presence of sufficient physiologically correct bulk helps stimulate intestinal motility and reestablish bowel regularity.

TO CORRECT YEARS OF
 CONSTIPATION WITH
 SOFT, MOIST, EASILY
 PASSED BULK



Cellothyl®

BRAND OF
 METHYLCYLLULOSE
 ESPECIALLY PREPARED
 BY THE
 CHILCOTT PROCESS



Cellothyl tablets (0.5 Gram) in bottles of 100, 500 and 5000.

CHILCOTT

Laboratories

DIVISION OF The Maltine Company

MORRIS PLAINS, NEW JERSEY

said. "I think every state in the nation will have a good representation of medical men. Doctors, perhaps more than any others, are aware that the existing competition for medical and technical manpower by the several federal hospital systems is depriving the general public of certain services to which they are entitled. They realize that this waste must be eliminated for the benefit of all our people."

The advisory committee has been formed to include high-ranking men in the 20 major divisions

of medicine and surgery and the allied technical skills, as follows:

Anesthesiology: Charles Fletcher McCuskey, M.D., Los Angeles, California; Dermatology and Syphilology: Donald M. Pillsbury, M.D., Philadelphia, Pennsylvania; General Practice: Samuel Arthur Garlan, M.D., New York, N. Y. and Rufus B. Robins, M.D., Camden, Arkansas; Internal Medicine: Maxwell Myer Wintrobe, M.D., Salt Lake City, Utah; Cardiology: George Edward Burch, M.D., New Orleans, Louisiana; Medical Education: Richard Hale Young,

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selective control of Gastrointestinal Spasm

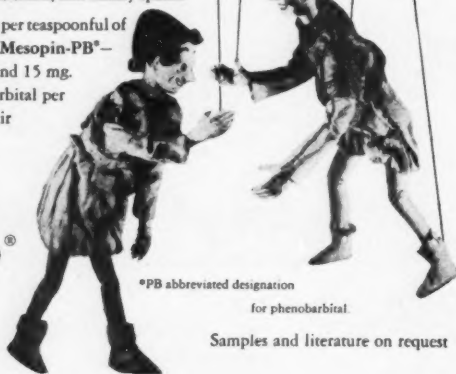
Mesopin®

(brand of homatropine methyl bromide)

When pain, heartburn, belching, nausea, or unstable colon are due to gastrointestinal spasm, Mesopin provides an effective means for prompt relief. Its selective antispasmodic action controls spasticity with virtual freedom from the undesirable side effects of atropine or belladonna. Thus, Mesopin is relatively safe for the relief of gastrointestinal spasticity, such as pylorospasm, cardiospasm, spastic colon, and biliary spasm.

Mesopin—2.5 mg. per teaspoonful of elixir or per tablet. Mesopin-PB*—2.5 mg. Mesopin and 15 mg. (1/4 gr.) phenobarbital per teaspoonful of elixir or per tablet.

Endo®



*PB abbreviated designation
for phenobarbital.

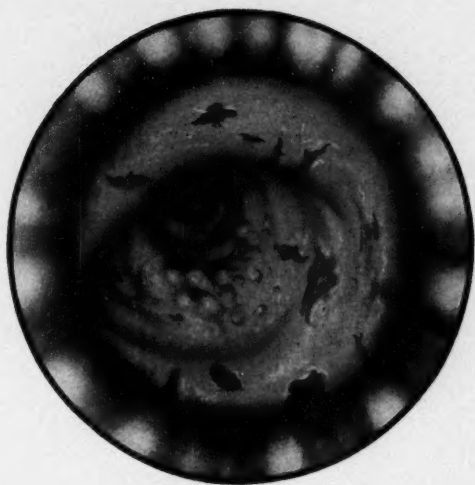
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Endo Products, Inc., Richmond Hill 18, N. Y.

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in dysentery due to Shigella paradysenteriae:

"Six children between the ages of four and six years . . . given terramycin. The diarrhea which was pronounced in each case stopped within 48 hours in the case of four patients and within 72 hours in the other two . . . In all cases, the organism disappeared from the stool after treatment was started and did not reappear."¹

Terramycin "is an effective agent in the chemotherapy of . . . chronic bacillary dysentery."²

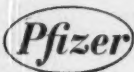
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available | Capsules, Elixir, Oral Drops, Intravenous,
Ophthalmic Ointment, Ophthalmic Solution.

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CHAS. PFIZER & CO., INC., Brooklyn 6, N. Y.



The Anticholinergic Action of Banthine in Peptic Ulcer

— reduces the excessive vagal stimulation characteristic of the ulcer diathesis by inhibiting stimuli at . . .

1. The parasympathetic and sympathetic ganglia.
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By this action Banthine consistently reduces hypermotility and, usually, hyperacidity.

Banthine[®]

BROMIDE

BRAND OF METHANTHELIN BROMIDE

Suggested Dosage:

One or two tablets
(50 to 100 mg.)
every six hours.

SEARLE RESEARCH IN THE SERVICE OF MEDICINE